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(54) Title: SUBSTITUTED N–ALIPHATIC–N–AROMATIC *TERTIARY*–HETEROALKYLAMINES USEFUL FOR INHIBITING CHOLESTERYL ESTER TRANSFER PROTEIN ACTIVITY

(57) Abstract

The invention relates to substituted N–Aliphatic–N–Aromatic *tertiary*–Heteroalkylamine compounds useful as inhibitors of cholesteryl ester transfer protein (CETP; plasma lipid transfer protein–I) and compounds, compositions and methods for treating atherosclerosis, dyslipidemia, and other coronary artery disease.

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Substituted N-Aliphatic-N-Aromatic*tertiary*-Heteroalkylamines Useful for Inhibiting Cholesteryl Ester Transfer Protein Activity

FIELD OF THE INVENTION

This invention is in the field of treating cardiovascular disease, and specifically relates to compounds, compositions and methods for treating atherosclerosis and other coronary artery disease. More particularly, the invention relates to substituted N-Aliphatic-N-Aromatic*tertiary*-Heteroalkylamine compounds that inhibit cholesteryl ester transfer protein (CETP), also known as plasma lipid transfer protein-I.

BACKGROUND OF THE INVENTION

Numerous studies have demonstrated that a low plasma concentration of high density lipoprotein (HDL) cholesterol is a powerful risk factor for the development of atherosclerosis (Barter and Rye, *Atherosclerosis*, 121, 1-12 (1996)). HDL is one of the major classes of lipoproteins that function in the transport of lipids through the blood. The major lipids found associated with HDL include cholesterol, cholesteryl ester, triglycerides, phospholipids and fatty acids. The other classes of lipoproteins found in the blood are low density lipoprotein (LDL) and very low density lipoprotein (VLDL). Since low levels of HDL cholesterol increase the risk of atherosclerosis, methods for elevating plasma HDL cholesterol would be therapeutically beneficial for the treatment of atherosclerosis and other diseases associated with accumulation of lipid in the blood vessels. These diseases include, but are not limited to, coronary heart disease, peripheral vascular disease, and stroke.

Atherosclerosis underlies most coronary artery disease (CAD), a major cause of morbidity and mortality in modern society. High LDL cholesterol (above 180 mg/dl) and low HDL cholesterol (below 35 mg/dl) have been shown to be important contributors to the development of atherosclerosis. Other diseases, such as peripheral vascular disease, stroke, and hypercholesterolaemia are negatively affected by adverse HDL/LDL ratios. Inhibition of CETP by the subject compounds is shown to effectively modify

plasma HDL/LDL ratios. and to check the progress and/or formation of these diseases.

CETP is a plasma protein that facilitates the movement of cholesteryl esters and triglycerides between the various lipoproteins in the blood (Tall, *J. Lipid Res.*, 34, 1255-74 (1993)). The movement of cholesteryl ester from HDL to LDL by CETP has the effect of lowering HDL cholesterol. It therefore follows that inhibition of CETP should lead to elevation of plasma HDL cholesterol and lowering of plasma LDL cholesterol, thereby providing a therapeutically beneficial plasma lipid profile (McCarthy, *Medicinal Res. Revs.*, 13, 139-59 (1993); Sitori, *Pharmac. Ther.*, 67,443-47 (1995)). This exact phenomenon was first demonstrated by Swenson et al., (*J. Biol. Chem.*, 264, 14318 (1989)) with the use of a monoclonal antibody that specifically inhibited CETP. In rabbits, the antibody caused an elevation of the plasma HDL cholesterol and a decrease in LDL cholesterol. Son et al. (*Biochim. Biophys. Acta* 795, 743-480 (1984)), Morton et al. (*J. Lipid Res.* 35, 836-847 (1994)) and Tollefson et al. (*Am. J. Physiol.*, 255, (Endocrinol. Metab. 18, E894-E902 (1988))) describe proteins from human plasma that inhibit CETP. U.S. Patent 5,519,001, issued to Kushwaha et al., describes a 36 amino acid peptide derived from baboon apo C-1 that inhibits CETP activity. Cho et al. (*Biochim. Biophys. Acta* 1391, 133-144 (1998)) describe a peptide from hog plasma that inhibits human CETP. Bonin et al. (*J. Peptide Res.*, 51, 216-225 (1998)) disclose a decapeptide inhibitor of CETP. A depsipeptide fungal metabolite is disclosed as a CETP inhibitor by Hedge et al. in *Bioorg. Med. Chem. Lett.*, 8, 1277-80 (1998).

There have been several reports of non-peptidic compounds that act as CETP inhibitors. Barrett et al. (*J. Am. Chem. Soc.*, 188, 7863-63 (1996)) and Kuo et al. (*J. Am. Chem. Soc.*, 117, 10629-34 (1995)) describe cyclopropane-containing CETP inhibitors. Pietzonka et al. (*Bioorg. Med. Chem. Lett*, 6, 1951-54 (1996)) describe phosphonate-containing analogs of cholesteryl ester as CETP inhibitors. Coval et al. (*Bioorg. Med. Chem. Lett.*, 5, 605-610 (1995)) describe Wiedendiol-A and -B, and related sesquiterpene compounds as CETP inhibitors. Japanese Patent Application No. 10287662-A describes polycyclic, non-amine containing, polyhydroxylic natural compounds possessing CETP inhibition properties. Lee et al. (*J. Antibiotics*, 49, 693-96 (1996)) describe CETP inhibitors derived from an insect fungus. Busch et al. (*Lipids*, 25, 216-220, (1990)) describe cholesteryl acetyl bromide

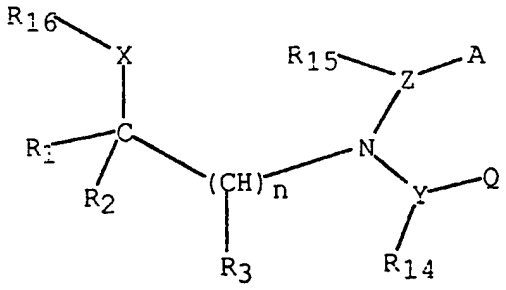
as a CETP inhibitor. Morton and Zilversmit (*J. Lipid Res.*, 35, 836-47 (1982)) describe that p-chloromercuriphenyl sulfonate, p-hydroxymercuribenzoate and ethyl mercurithiosalicylate inhibit CETP. Connolly et al. (*Biochem. Biophys. Res. Comm.* 223, 42-47 (1996)) describe other cysteine modification reagents as CETP inhibitors. Xia et al. describe 1,3,5-triazines as CETP inhibitors (Bioorg. Med. Chem. Lett., 6, 919-22 (1996)). Bisgaier et al. (*Lipids*, 29, 811-8 (1994)) describe 4-phenyl-5-tridecyl-4H-1,2,4-triazole-thiol as a CETP inhibitor. Oomura et al. disclose non-peptidic tetracyclic and hexacyclic phenols as CETP inhibitors in Japanese Patent Application No. 10287662. In WO Patent Application No. 09914204, Sikorski describes 1,2,4-triazolylthiols useful as chlolesteryl ester transfer protein inhibitors.

Some substituted heteroalkylamine compounds are known. In European Patent Application No. 796846, Schmidt et al. describe 2-aryl-substituted pyridines as cholesteryl ester transfer protein inhibitors useful as cardiovascular agents. One substitutent at C3 of the pyridine ring can be an hydroxyalkyl group. In European Patent Application No. 801060, Dow and Wright describe heterocyclic derivatives substituted with an aldehyde addition product of an alkylamine to afford 1-hydroxy-1-amines. These are reported to be β3-adrenergic receptor agonists useful for treating diabetes and other disorders. In Great Britain Patent Application No. 2305665, Fisher et al. disclose 3-agonist secondary amino alcohol substituted pyridine derivatives useful for treating several disorders including cholesterol levels and artherosclerotic diseases. In European Patent Application No. 818448, Schmidt et al. describe tetrahydroquinoline derivatives as chlolesteryl ester transfer protein inhibitors. European Patent Application No. 818197, Schmek et al. describe pyridines with fused heterocycles as cholesteryl ester transfer protein inhibitors. Brandes et al. in German Patent Application No. 19627430 describe bicyclic condensed pyridine derivatives as cholesteryl ester transfer protein inhibitors. In WO Patent Application No. 09839299, Muller-Gliemann et al. describe quinoline derivatives as cholesteryl ester transfer protein inhibitors. U.S. Patent 2,700,686, issued to Dickey and Towne, describes N-(2-haloalkyl-2-hydroxyethyl)amines in which the amine is further substituted with either 1 to 2 aliphatic groups or one aromatic group and one aliphatic group. U.S. Patent 2.700,686 further describes a process to prepare the N-(2-

haloalkyl-2-hydroxyethyl)amines by reacting halogenated-1,2-epoxyalkanes with the corresponding aliphatic amines and N-alkylanilines and their use as dye intermediates.

SUMMARY OF THE INVENTION

The present invention provides a class of compounds that can be used to inhibit cholesteryl ester transfer protein (CETP) activity and that have the general structure:



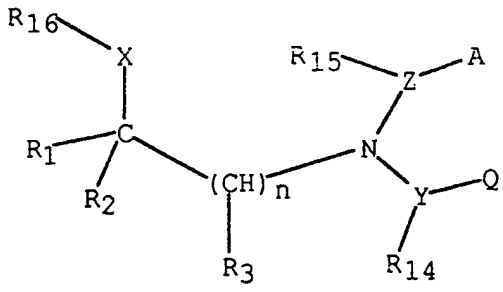
In another aspect , the present invention includes pharmaceutical compositions comprising a pharmaceutically effective amount of the compounds of this invention and a pharmaceutically acceptable carrier.

In another aspect, this invention relates to methods of using these inhibitors as therapeutic agents in humans to inhibit cholesteryl ester transfer protein (CETP) activity, thereby decreasing the concentrations of low density lipoprotein (LDL) and raising the level of high density lipoprotein (HDL), resulting in a therapeutically beneficial plasma lipid profile. The compounds and methods of this invention can also be used to treat dyslipidemia (hypoalphalipoproteinemia), hyperlipoproteinaemia (chylomicronemia and hyperapobetalipoproteinemia), peripheral vascular disease, hypercholesterolaemia, atherosclerosis, coronary artery disease and other CETP-mediated disorders. The compounds can also be used in prophylactic treatment of subjects who are at risk of developing such disorders. The compounds can be used to lower the risk of atherosclerosis. The compounds of this invention would be also useful in prevention of cerebral vascular accident (CVA) or stroke. Besides being useful for human treatment, these

compounds are also useful for veterinary treatment of companion animals, exotic animals and farm animals such as primates, rabbits, pigs, horses, and the like.

DESCRIPTION OF THE INVENTION

The present invention relates to a class of compounds comprising substituted N-Aliphatic-N-Aromatic*tertiary*-Heteroalkylamines which are beneficial in the therapeutic and prophylactic treatment of coronary artery disease as given in Formula I-WA (also referred to herein as "alicyclic/cyclic aryl/heteroaryl heteroalkylamines"):



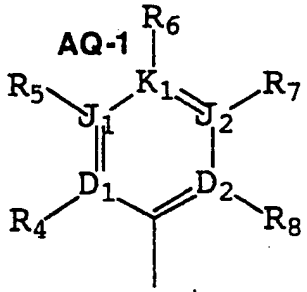
(I-WA)

or a pharmaceutically-acceptable salt thereof, wherein;

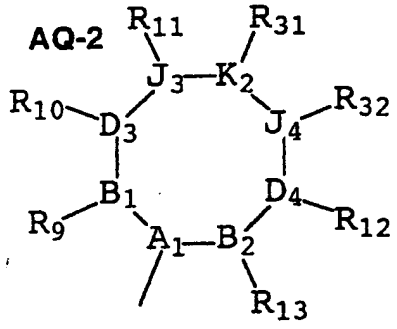
n is an integer selected from 1 through 4;

A and Q are independently selected from the group consisting of

$-CH_2(CR_{37}R_{38})_v-(CR_{33}R_{34})_u-T-(CR_{35}R_{36})_w-H$,



and



with the provisos that one of A and Q must be AQ-1 and that one of A and Q must be selected from the group consisting of AQ-2 and

$-CH_2(CR_{37}R_{38})_v-(CR_{33}R_{34})_u-T-(CR_{35}R_{36})_w-H$;

T is selected from the group consisting of a single covalent bond, O, S, S(O), $S(O)_2$, $C(R_{33})=C(R_{35})$, and C≡C;

v is an integer selected from 0 through 1 with the proviso that v is 1 when any one of R_{33}, R_{34}, R_{35}, and R_{36} is aryl or heteroaryl;

u and w are integers independently selected from 0 through 6;

A_1 is $C(R_{30})$;

D_1, D_2, J_1, J_2 and K_1 are independently selected from the group consisting of C, N, O, S and a covalent bond with the provisos that no more than one of D_1, D_2, J_1, J_2 and K_1 is a covalent bond, no more than one of D_1, D_2, J_1, J_2 and K_1 is O, no more than one of D_1, D_2, J_1, J_2 and K_1 is S, one of D_1, D_2, J_1, J_2 and K_1 must be a covalent bond when two of D_1, D_2, J_1, J_2 and K_1 are O and S, and no more than four of D_1, D_2, J_1, J_2 and K_1 are N;

B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are independently selected from the group consisting of C, $C(R_{30})$, N, O, S and a covalent bond with the provisos that no more than 5 of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are a covalent bond, no more than two of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are O, no more than two of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are S, no more than two of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are simultaneously O and S, and no more than two of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are N;

B_1 and D_3, D_3 and J_3, J_3 and K_2, K_2 and J_4, J_4 and D_4, and D_4 and B_2 are independently selected to form an in-ring spacer pair wherein said spacer pair is selected from the group consisting of $C(R_{33})=C(R_{35})$ and N=N with the provisos that AQ-2 must be a ring of at least five contiguous members,

that no more than two of the group of said spacer pairs are simultaneously $C(R_{33})=C(R_{35})$, and that no more than one of the group of said spacer pairs can N=N unless the other spacer pairs is other than $C(R_{33})=C(R_{35})$, O, N, and S;

R_{16} is selected from the group consisting of hydrido, alkyl, acyl, aroyl, heteroaroyl, and trialkylsilyl;

X is selected from the group consisting of O, H, F, S, S(O), NH, N(OH), N(alkyl), and N(alkoxy) with the proviso that there is no R_{16} wherein X is H or F;

R_1 is selected from the group consisting of haloalkyl, haloalkenyl, haloalkoxyalkyl, and haloalkenyloxyalkyl;

R_2 is selected from the group consisting of hydrido, aryl, aralkyl, alkyl, alkenyl, alkenyloxyalkyl, haloalkyl, haloalkenyl, halocycloalkyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, halocycloalkoxy, halocycloalkoxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, heteroaryl, dicyanoalkyl, and carboalkoxycyanoalkyl;

R_3 is selected from the group consisting of hydrido, hydroxy, cyano, aryl, aralkyl, acyl, alkoxy, alkyl, alkenyl, alkoxyalkyl, heteroaryl, alkenyloxyalkyl, haloalkyl, haloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, monocyanoalkyl, dicyanoalkyl, carboxamide, and carboxamidoalkyl;

Y is selected from a group consisting of a covalent single bond, $(C(R_{14})2)_q$ wherein q is an integer selected from 1 through 4 and $(CH(R_{14}))_g$-O-$(CH(R_{14}))_p$ wherein g and p are integers independently selected from 0 through 2;

R_{14} is selected from the group consisting of hydrido, hydroxy, cyano, hydroxyalkyl, acyl, alkoxy, alkyl, alkenyl, alkynyl, alkoxyalkyl, haloalkyl, haloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl,

monocarboalkoxyalkyl, monocyanoalkyl, dicyanoalkyl, carboalkoxycyanoalkyl, carboalkoxy, carboxamide, carboxamidoalkyl;

Z is selected from the group consisting of covalent single bond, $(C(R_{15})_2)_q$ wherein q is an integer selected from 1 through 2, and $(CH(R_{15}))_j$-O-$(CH(R_{15}))_k$ wherein j and k are integers independently selected from 0 through 2;

R_{15} is selected from the group consisting of hydrido, cyano, hydroxyalkyl, acyl, alkoxy, alkyl, alkenyl, alkynyl, alkoxyalkyl, haloalkyl, haloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, monocarboalkoxyalkyl, monocyanoalkyl, dicyanoalkyl, carboalkoxycyanoalkyl, carboalkoxy, carboxamide, and carboxamidoalkyl;

R_{30} is selected from the group consisting of hydrido, alkoxy, alkoxyalkyl, halo, haloalkyl, alkylamino, alkylthio, alkylthioalkyl, alkyl, alkenyl, haloalkoxy, and haloalkoxyalkyl with the proviso that R_{30} is selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen;

R_{30}, when bonded to A_1, is taken together to form an intra-ring linear spacer connecting the A_1-carbon at the point of attachment of R_{30} to the point of bonding of a group selected from the group consisting of R_{10}, R_{11}, R_{12}, R_{31}, and R_{32} wherein said intra-ring linear spacer is selected from the group consisting of a covalent single bond and a spacer moiety having from 1 through 6 contiguous atoms to form a ring selected from the group consisting of a cycloalkyl having from 3 through 10 contiguous members, a cycloalkenyl having from 5 through 10 contiguous members, and a heterocyclyl having from 5 through 10 contiguous members;

R_{30}, when bonded to A_1, is taken together to form an intra-ring branched spacer connecting the A_1-carbon at the point of attachment of R_{30} to the points of bonding of each member of any one of substituent pairs selected

from the group consisting of subsitituent pairs R_{10} and R_{11}, R_{10} and R_{31}, R_{10} and R_{32}, R_{10} and R_{12}, R_{11} and R_{31}, R_{11} and R_{32}, R_{11} and R_{12}, R_{31} and R_{32}, R_{31} and R_{12}, and R_{32} and R_{12} and wherein said intra-ring branched spacer is selected to form two rings selected from the group consisting of cycloalkyl having from 3 through 10 contiguous members, cycloalkenyl having from 5 through 10 contiguous members, and heterocyclyl having from 5 through 10 contiguous members;

R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, R_{32} , R_{33}, R_{34}, R_{35}, and R_{36} are independently selected from the group consisting of hydrido, carboxy, heteroaralkylthio, heteroaralkoxy, cycloalkylamino, acylalkyl, acylalkoxy, aroylalkoxy, heterocyclyloxy, aralkylaryl, aralkyl, aralkenyl, aralkynyl, heterocyclyl, perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, aralkylsulfinyl, aralkylsulfinylalkyl, halocycloalkyl, halocycloalkenyl, cycloalkylsulfinyl, cycloalkylsulfinylalkyl, cycloalkylsulfonyl, cycloalkylsulfonylalkyl, heteroarylamino, N-heteroarylamino-N-alkylamino, heteroarylaminoalkyl,haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, haloalkoxylalkyl, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, cycloalkoxyalkyl, cycloalkylalkoxy, cycloalkenyloxyalkyl, cycloalkylenedioxy, halocycloalkoxy, halocycloalkoxyalkyl, halocycloalkenyloxy, halocycloalkenyloxyalkyl, hydroxy, amino, thio, nitro, lower alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylthioalkyl, heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, arylsulfonylalkyl, heteroarylsulfinylalkyl, heteroarylsulfonylalkyl, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfinylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, monoarylamidosulfonyl, arylsulfonamido, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, heterocyclylsulfonyl, heterocyclylthio, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, alkenyloxy, alkenyloxyalky, alkylenedioxy, haloalkylenedioxy,

cycloalkyl, cycloalkylalkanoyl. cycloalkenyl, lower cycloalkylalkyl, lower cycloalkenylalkyl, halo, haloalkyl, haloalkenyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydoxyheteroaralkyl, haloalkoxyalkyl, aryl, heteroaralkynyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, arylalkenyl, heteroarylalkenyl, carboxyalkyl, carboalkoxy, alkoxycarboxamido, alkylamidocarbonylamido, arylamidocarbonylamido, carboalkoxyalkyl, carboalkoxyalkenyl, carboaralkoxy, carboxamido, carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl with the provisos that R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, R_{32} , R_{33}, R_{34}, R_{35}, and R_{36} are each independently selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen, that no more than three of the R_{33} and R_{34} substituents are simultaneously selected from other than the group consisting of of hydrido and halo, and that no more than three of the R_{35} and R_{36} substituents are simultaneously selected from other than the group consistubg of hydrido and halo;

R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, and R_{32} are independently selected to be oxo with the provisos that B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are independently selected from the group consisting of C and S, no more than two of R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, and R_{32} are simultaneously oxo, and that R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, and R_{32} are each independently selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen;

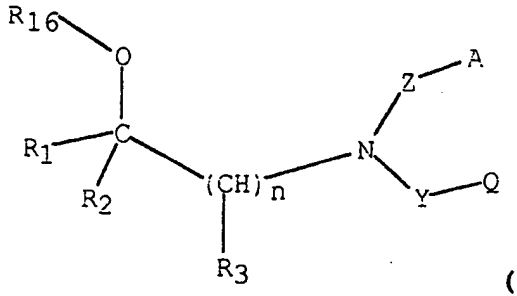
R_4 and R_5, R_5 and R_6, R_6 and R_7, R_7 and R_8, R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{31}, R_{31} and R_{32}, R_{32} and R_{12}, and R_{12} and R_{13} are independently selected to form spacer pairs wherein a spacer pair is taken together to form a linear moiety having from 3 through 6 contiguous atoms

connecting the points of bonding of said spacer pair members to form a ring selected from the group consisting of a cycloalkenyl ring having 5 through 8 contiguous members, a partially saturated heterocyclyl ring having 5 through 8 contiguous members, a heteroaryl ring having 5 through 6 contiguous members, and an aryl with the provisos that no more than one of the group consisting of spacer pairs R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8, are used at the same time and that no more than one of the group consisting of spacer pairs R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{31}, R_{31} and R_{32}, R_{32} and R_{12}, and R_{12} and R_{13} are used at the same time;

R_9 and R_{11}, R_9 and R_{12}, R_9 and R_{13}, R_9 and R_{31}, R_9 and R_{32}, R_{10} and R_{12}, R_{10} and R_{13}, R_{10} and R_{31}, R_{10} and R_{32}, R_{11} and R_{12}, R_{11} and R_{13}, R_{11} and R_{32}, R_{12} and R_{31}, R_{13} and R_{31}, and R_{13} and R_{32} are independently selected to form a spacer pair wherein said spacer pair is taken together to form a linear spacer moiety selected from the group consisting of a covalent single bond and a moiety having from 1 through 3 contiguous atoms to form a ring selected from the group consisting of a cycloalkyl having from 3 through 8 contiguous members, a cycloalkenyl having from 5 through 8 contiguous members, a saturated heterocyclyl having from 5 through 8 contiguous members and a partially saturated heterocyclyl having from 5 through 8 contiguous members with the provisos that no more than one of said group of spacer pairs is used at the same time:

R_{37} and R_{38} are independently selected from the group consisting of hydrido, alkoxy, alkoxyalkyl, hydroxy, amino, thio, halo, haloalkyl, alkylamino, alkylthio, alkylthioalkyl, cyano, alkyl, alkenyl, haloalkoxy, and haloalkoxyalkyl.

In another embodiment of compounds of Formula I-WA, compounds are alcohols and have the Formula I-WO (also referred to herein as "alicyclic/cyclic aryl/heteroaryl aminoalkanols"):



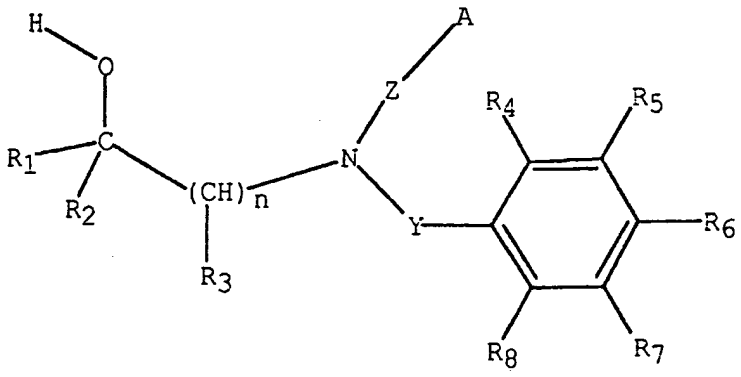
(I-WO)

or a pharmaceutically acceptable salt thereof, wherein;

R_{16} is hydrido;

R_1, R_2, R_3, n, A, Y, Q, and Z are defined as given above for Formula I-WA.

In a more specific embodiment of compounds of Formula I-WO, compounds have the Formula I-WOPA:



(I-WOPA)

or a pharmaceutically acceptable salt thereof, wherein;

n is an integer selected from 1 through 2;

A is selected from the group consisting of C3-C8 alkyl, C3-C8 alkenyl, C3-C8 alkynyl, C3-C8 haloalkyl, C3-C8 haloalkenyl, C3-C6 alkoxy C1-C2 alkyl, and C3-C8 hydroxyhaloalkyl, wherein each member of group A may be optionally substituted at any carbon up to and including 6 atoms from the point of attachment of A to Z with one or more of the group consisting of

R_{33}, R_{34}, R_{35}, and R_{36} with the provisos that R_{33}, R_{34}, R_{35}, and R_{36} must not be attached to the carbon directly linking A to Z and that R_{33}, R_{34}, R_{35}, and R_{36} must be selected from other than aryl and heteroaryl when substituting the carbon 2 atoms from Z wherein Z is a single covalent bond;

R_1 is selected from the group consisting of haloalkyl and haloalkoxymethyl;

R_2 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, haloalkoxy, haloalkoxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, and heteroaryl;

R_3 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, and haloalkoxyalkyl;

Y and Z are independently selected from the group consisting of a covalent single bond, oxy and alkylene;

R_4 and R_8 are independently selected from the group consisting of hydrido and halo;

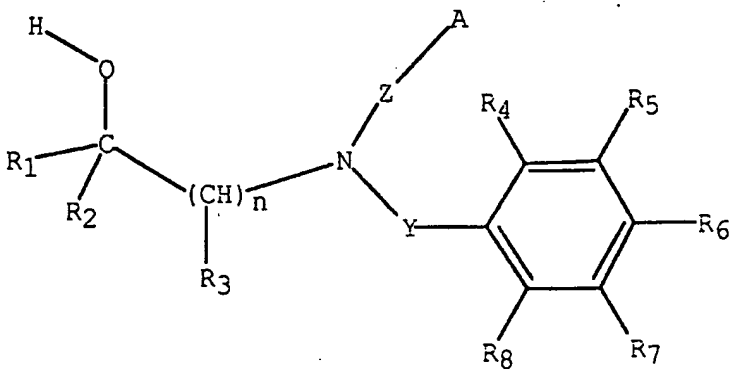
R_5, R_6, and R_7 are independently selected from the group consisting of hydrido, alkyl, halo, haloalkyl, haloalkoxy, aryl, alkylthio, arylamino, arylthio, aroyl, arylsulfonyl, aryloxy, aralkoxy, heteroaryloxy, alkoxy, aralkyl, cycloalkoxy, cycloalkylalkoxy, cycloalkylalkanoyl, heteroaryl, cycloalkyl, haloalkylthio, hydroxyhaloalkyl, heteroaralkoxy, heterocyclyloxy, aralkylaryl, heteroaryloxyalkyl, heteroarylthio, and heteroarylsulfonyl;

R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8 are independently selected to form spacer pairs wherein a spacer pair is taken together to form a linear moiety having from 3 through 6 contiguous atoms connecting the points of bonding of said spacer pair members to form a ring selected from the group consisting of a cycloalkenyl ring having 5 through 8 contiguous members, a partially saturated heterocyclyl ring having 5 through 8 contiguous members, a heteroaryl ring having 5 through 6 contiguous members, and an aryl with the

proviso that no more than one of the group consisting of spacer pairs R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8, is used at the same time;

R_{33}, R_{34}, R_{35}, and R_{36} are independently selected from the group group consisting of alkyl, halo, hydroxy, cyano, haloalkyl, haloalkoxy, aryl, alkylthio, arylamino, arylthio, aroyl, arylsulfonyl, aryloxy, aralkoxy, heteroaryloxy, alkoxy, aralkyl, cycloalkoxy, cycloalkylalkoxy, cycloalkylalkanoyl, heteroaryl, cycloalkyl, haloalkylthio, hydroxyhaloalkyl, heteroaralkoxy, heterocyclyloxy, aralkylaryl, heteroaryloxyalkyl, heteroarylthio, and heteroarylsulfonyl.

In another more specific embodiment of compounds of Formula I-WO, compounds have the Formula I-WOPC:



(I-WOPC)

or a pharmaceutically acceptable salt thereof, wherein;

n is an integer selected from 1 through 2;

A is selected from the group consisting of C3-C10 cycloalkyl, C5-C10 cycloalkenyl, C4-C9 saturated heterocyclyl, and C4-C9 partially saturated heterocyclyl, wherein each ring carbon may be optionally substituted with R_{30}, a ring carbon other than the ring carbon at the point of attachment of A to Z may be optionally substituted with oxo provided that no more than one ring carbon is substituted by oxo at the same time, ring carbon and nitrogen atoms adjacent to the carbon atom at the point of attachment may be optionally substituted with R_9 or R_{13}, a ring carbon or nitrogen atom adjacent to the R_9

position and two atoms from the point of attachment may be substituted with R_{10}, a ring carbon or nitrogen atom adjacent to the R_{13} position and two atoms from the point of attachment may be substituted with R_{12}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{10} position may be substituted with R_{11}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{12} position may be substituted with R_{32}, and a ring carbon or nitrogen atom four atoms from the point of attachment and adjacent to the R_{11} and R_{32} positions may be substituted with R_{31};

R_1 is selected from the group consisting of haloalkyl and haloalkoxymethyl;

R_2 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, haloalkoxy, haloalkoxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, and heteroaryl;

R_3 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, and haloalkoxyalkyl;

Y and Z are independently selected from the group consisting of a covalent single bond, oxy and alkylene;

R_4 and R_8 are independently selected from the group consisting of hydrido and halo;

R_9 and R_{13} is halo;

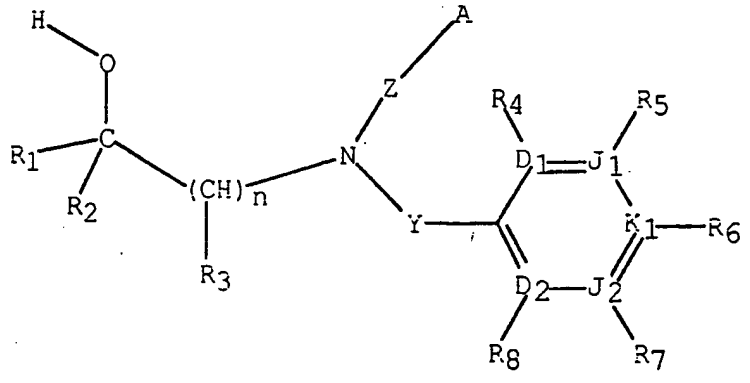
R_5, R_6, and R_7 are independently selected from the group consisting of hydrido, alkyl, halo, haloalkyl, haloalkoxy, aryl, alkylthio, arylamino, arylthio, aroyl, arylsulfonyl, aryloxy, aralkoxy, heteroaryloxy, alkoxy, aralkyl, cycloalkoxy, cycloalkylalkoxy, cycloalkylalkanoyl, heteroaryl, cycloalkyl, haloalkylthio, hydroxyhaloalkyl, heteroaralkoxy, heterocyclyloxy, aralkylaryl, heteroaryloxyalkyl, heteroarylthio, and heteroarylsulfonyl;

R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8 are independently selected to form spacer pairs wherein a spacer pair is taken together to form a linear moiety having from 3 through 6 contiguous atoms connecting the points of bonding of said spacer pair members to form a ring selected from the group consisting of a cycloalkenyl ring having 5 through 8 contiguous members, a partially saturated heterocyclyl ring having 5 through 8 contiguous members, a heteroaryl ring having 5 through 6 contiguous members, and an aryl with the proviso that no more than one of the group consisting of spacer pairs R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8, is used at the same time;

R_{10}, R_{11}, R_{12}, R_{31}, and R_{32} are independently selected from the group group consisting of alkyl, halo, haloalkyl, haloalkoxy, aryl, alkylthio, arylamino, arylthio, aroyl, arylsulfonyl, aryloxy, aralkoxy, heteroaryloxy, alkoxy, aralkyl, cycloalkoxy, cycloalkylalkoxy, cycloalkylalkanoyl, heteroaryl, cycloalkyl, haloalkylthio, hydroxyhaloalkyl, heteroaralkoxy, heterocyclyloxy, aralkylaryl, heteroaryloxyalkyl, heteroarylthio, and heteroarylsulfonyl;

R_{30} is selected from the group consisting of alkoxy, alkoxyalkyl, halo, haloalkyl, alkylamino, alkylthio, alkylthioalkyl, alkyl, alkenyl, haloalkoxy, and haloalkoxyalkyl.

In another more specific embodiment of compounds of Formula I-WO, compounds have the Formula I-WOHA:



(I-WOHA)

or a pharmaceutically acceptable salt thereof, wherein;

n is an integer selected from 1 through 2;

A is selected from the group consisting of C3-C8 alkyl, C3-C8 alkenyl, C3-C8 alkynyl, C3-C8 haloalkyl, C3-C8 haloalkenyl, C3-C6 alkoxy C1-C2 alkyl, and C3-C8 hydroxyhaloalkyl, wherein each member of group A may be optionally substituted at any carbon up to and including 6 atoms from the point of attachment of A to Z with one or more of the group consisting of R_{33}, R_{34}, R_{35}, and R_{36} with the provisos that R_{33}, R_{34}, R_{35}, and R_{36} must not be attached to the carbon directly linking A to Z and that R_{33}, R_{34}, R_{35}, and R_{36} must be selected from other than aryl and heteroaryl when substituting the carbon 2 atoms from Z wherein Z is a single covalent bond;

D_1, D_2, J_1, J_2 and K_1 are independently selected from the group consisting of C, N, O, S and a covalent bond with the provisos that no more than one of D_1, D_2, J_1, J_2 and K_1 is a covalent bond, no more than one of D_1, D_2, J_1, J_2 and K_1 is O, no more than one of D_1, D_2, J_1, J_2 and K_1 is S, one of D_1, D_2, J_1, J_2 and K_1 must be a covalent bond when two of D_1, D_2, J_1, J_2 and K_1 are O and S, and no more than four of D_1, D_2, J_1, J_2 and K_1 are N;

R_1 is selected from the group consisting of haloalkyl and haloalkoxymethyl;

R_2 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, haloalkoxy, haloalkoxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, and heteroaryl;

R_3 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, and haloalkoxyalkyl;

Y and Z are independently selected from the group consisting of a covalent single bond, oxy and alkylene;

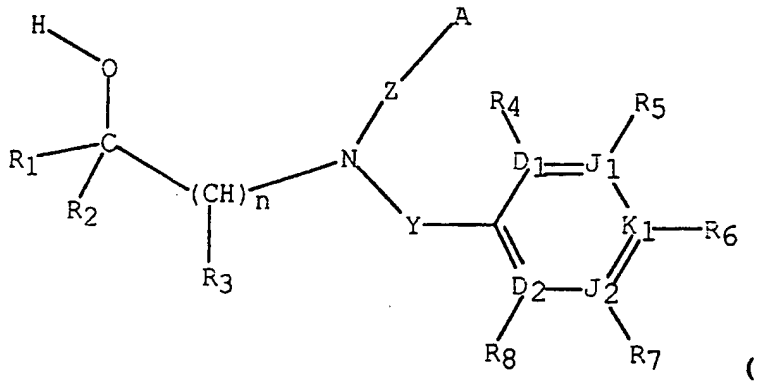
R_4 and R_8 are independently selected from the group consisting of hydrido and halo;

R_5, R_6, and R_7 are independently selected from the group consisting of hydrido, alkyl, halo, haloalkyl, haloalkoxy, aryl, alkylthio, arylamino, arylthio, aroyl, arylsulfonyl, aryloxy, aralkoxy, heteroaryloxy, alkoxy, aralkyl, cycloalkoxy, cycloalkylalkoxy, cycloalkylalkanoyl, heteroaryl, cycloalkyl, haloalkylthio, hydroxyhaloalkyl, heteroaralkoxy, heterocyclyloxy, aralkylaryl, heteroaryloxyalkyl, heteroarylthio, and heteroarylsulfonyl;

R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8 are independently selected to form spacer pairs wherein a spacer pair is taken together to form a linear moiety having from 3 through 6 contiguous atoms connecting the points of bonding of said spacer pair members to form a ring selected from the group consisting of a cycloalkenyl ring having 5 through 8 contiguous members, a partially saturated heterocyclyl ring having 5 through 8 contiguous members, a heteroaryl ring having 5 through 6 contiguous members, and an aryl with the proviso that no more than one of the group consisting of spacer pairs R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8, is used at the same time;

R_{33}, R_{34}, R_{35}, and R_{36} are independently selected from the group group consisting of alkyl, halo, hydroxy, cyano, haloalkyl, haloalkoxy, aryl, alkylthio, arylamino, arylthio, aroyl, arylsulfonyl, aryloxy, aralkoxy, heteroaryloxy, alkoxy, aralkyl, cycloalkoxy, cycloalkylalkoxy, cycloalkylalkanoyl, heteroaryl, cycloalkyl, haloalkylthio, hydroxyhaloalkyl, heteroaralkoxy, heterocyclyloxy, aralkylaryl, heteroaryloxyalkyl, heteroarylthio, and heteroarylsulfonyl.

In still another more specific embodiment of compounds of Formula I-WO, compounds have the Formula I-WOHC:



(I-WOHC)

or a pharmaceutically acceptable salt thereof, wherein;

n is an integer selected from 1 through 2;

A is selected from the group consisting of C3-C10 cycloalkyl, C5-C10 cycloalkenyl, C4-C9 saturated heterocyclyl, and C4-C9 partially saturated heterocyclyl, wherein each ring carbon may be optionally substituted with R_{30}, a ring carbon other than the ring carbon at the point of attachment of A to Z may be optionally substituted with oxo provided that no more than one ring carbon is substituted by oxo at the same time, ring carbon and nitrogen atoms adjacent to the carbon atom at the point of attachment may be optionally substituted with R_9 or R_{13}, a ring carbon or nitrogen atom adjacent to the R_9 position and two atoms from the point of attachment may be substituted with R_{10}, a ring carbon or nitrogen atom adjacent to the R_{13} position and two atoms from the point of attachment may be substituted with R_{12}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{10} position may be substituted with R_{11}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{12} position may be substituted with R_{32}, and a ring carbon or nitrogen atom four atoms from

the point of attachment and adjacent to the R_{11} and R_{32} positions may be substituted with R_{31};

D_1, D_2, J_1, J_2 and K_1 are independently selected from the group consisting of C, N, O, S and a covalent bond with the provisos that no more than one of D_1, D_2, J_1, J_2 and K_1 is a covalent bond, no more than one of D_1, D_2, J_1, J_2 and K_1 is O, no more than one of D_1, D_2, J_1, J_2 and K_1 is S, one of D_1, D_2, J_1, J_2 and K_1 must be a covalent bond when two of D_1, D_2, J_1, J_2 and K_1 are O and S, and no more than four of D_1, D_2, J_1, J_2 and K_1 are N;

R_1 is selected from the group consisting of haloalkyl and haloalkoxymethyl;

R_2 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, haloalkoxy, haloalkoxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, and heteroaryl;

R_3 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, and haloalkoxyalkyl;

Y and Z are independently selected from the group consisting of a covalent single bond, oxy and alkylene;

R_4 and R_8 are independently selected from the group consisting of hydrido and halo;

R_9 and R_{13} is halo;

R_5, R_6, and R_7 are independently selected from the group consisting of hydrido, alkyl, halo, haloalkyl, haloalkoxy, aryl, alkylthio, arylamino, arylthio, aroyl, arylsulfonyl, aryloxy, aralkoxy, heteroaryloxy, alkoxy, aralkyl, cycloalkoxy, cycloalkylalkoxy, cycloalkylalkanoyl, heteroaryl, cycloalkyl, haloalkylthio, hydroxyhaloalkyl, heteroaralkoxy, heterocyclyloxy, aralkylaryl, heteroaryloxyalkyl, heteroarylthio, and heteroarylsulfonyl;

R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8 are independently selected to form spacer pairs wherein a spacer pair is taken together to form a linear moiety having from 3 through 6 contiguous atoms connecting the points of bonding of said spacer pair members to form a ring selected from the group consisting of a cycloalkenyl ring having 5 through 8 contiguous members, a partially saturated heterocyclyl ring having 5 through 8 contiguous members, a heteroaryl ring having 5 through 6 contiguous members, and an aryl with the proviso that no more than one of the group consisting of spacer pairs R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8, is used at the same time;

R_{10}, R_{11}, R_{12}, R_{31}, and R_{32} are independently selected from the group group consisting of alkyl, halo, haloalkyl, haloalkoxy, aryl, alkylthio, arylamino, arylthio, aroyl, arylsulfonyl, aryloxy, aralkoxy, heteroaryloxy, alkoxy, aralkyl, cycloalkoxy, cycloalkylalkoxy, cycloalkylalkanoyl, heteroaryl, cycloalkyl, haloalkylthio, hydroxyhaloalkyl, heteroaralkoxy, heterocyclyloxy, aralkylaryl, heteroaryloxyalkyl, heteroarylthio, and heteroarylsulfonyl;

R_{30} is selected from the group consisting of alkoxy, alkoxyalkyl, halo, haloalkyl, alkylamino, alkylthio, alkylthioalkyl, alkyl, alkenyl, haloalkoxy, and haloalkoxyalkyl.

In a preferred specific embodiment of compounds of Formulas I-WOPA, I-WOHA, I-WOPC, and I-WOHC,

n is the integer 1;

R_1 is selected from the group consisting of trifluoromethyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, difluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

R_2 is selected from the group consisting of hydrido, methyl, ethyl, propyl, butyl, vinyl, phenyl, 4-trifluoromethylphenyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, difluoromethyl, pentafluoroethyl, trifluoromethyl, and 2,2,3,3,3-pentafluoropropyl;

R_3 is selected from the group consisting of hydrido, phenyl, 4-trifluoromethylphenyl, methyl, ethyl, vinyl, trifluoromethyl, trifluoromethoxymethyl, difluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

Y and Z are independently selected from the group consisting of a covalent single bond, oxy, and methylene with the proviso that only one of Y and Z are simultaneously oxy;

R_4 and R_8 are independently selected from the group consisting of hydrido and fluoro;

R_5 is selected from the group consisting of 4-aminophenoxy, benzoyl, benzyl, benzyloxy, 5-bromo-2-fluorophenoxy, 4-bromo-3-fluorophenoxy, 4-bromo-2-nitrophenoxy, 3-bromobenzyloxy, 4-bromobenzyloxy, 4-bromophenoxy, 5-bromopyrid-2-yloxy, 4-butoxyphenoxy, chloro, 3-chlorobenzyl, 2-chlorophenoxy, 4-chlorophenoxy, 4-chloro-3-ethylphenoxy, 3-chloro-4-fluorobenzyl, 3-chloro-4-fluorophenyl, 3-chloro-2-fluorobenzyloxy, 3-chlorobenzyloxy, 4-chlorobenzyloxy, 4-chloro-3-methylphenoxy, 2-chloro-4-fluorophenoxy, 4-chloro-2-fluorophenoxy, 4-chlorophenoxy, 3-chloro-4-ethylphenoxy, 3-chloro-4-methylphenoxy, 3-chloro-4-fluorophenoxy, 4-chloro-3-fluorophenoxy, 4-chlorophenylamino, 5-chloropyrid-3-yloxy, 2-cyanopyrid-3-yloxy, 4-cyanophenoxy, cyclobutoxy, cyclobutyl, cyclohexoxy, cyclohexylmethoxy, cyclopentoxy, cyclopentyl, cyclopentylcarbonyl, cyclopropyl, cyclopropylmethoxy, cyclopropoxy, 2,3-dichlorophenoxy, 2,4-dichlorophenoxy, 2,4-dichlorophenyl, 3,5-dichlorophenyl, 3,5-dichlorobenzyl, 3,4-dichlorophenoxy, 3,4-difluorophenoxy, 2,3-difluorobenzyloxy, 2,4-difluorobenzyloxy, 3,4-difluorobenzyloxy, 2,5-difluorobenzyloxy, 3,5-difluorophenoxy, 3,4-difluorophenyl, 3,5-difluorobenzyloxy, 4-difluoromethoxybenzyloxy, 2,3-difluorophenoxy, 2,4-difluorophenoxy, 2,5-difluorophenoxy, 3,5-dimethoxyphenoxy, 3-dimethylaminophenoxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 3,4-dimethylbenzyl, 3,4-dimethylbenzyloxy, 3,5-dimethylbenzyloxy, 2,2-dimethylpropoxy, 1,3-dioxan-2-yl, 1,4-dioxan-2-yl, 1,3-dioxolan-2-yl, ethoxy, 4-ethoxyphenoxy,

4-ethylbenzyloxy, 3-ethylphenoxy, 4-ethylaminophenoxy, 3-ethyl-5-methylphenoxy, fluoro, 4-fluoro-3-methylbenzyl, 4-fluoro-3-methylphenyl, 4-fluoro-3-methylbenzoyl, 4-fluorobenzyloxy, 2-fluoro-3-methylphenoxy, 3-fluoro-4-methylphenoxy, 3-fluorophenoxy, 3-fluoro-2-nitrophenoxy, 2-fluoro-3-trifluoromethylbenzyloxy, 3-fluoro-5-trifluoromethylbenzyloxy, 4-fluoro-2-trifluoromethylbenzyloxy, 4-fluoro-3-trifluoromethylbenzyloxy, 2-fluorophenoxy, 4-fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2-fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4-trifluoromethylphenoxy, 4-fluoropyrid-2-yloxy, 2-furyl, 3-furyl, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, 2-hydroxy-3,3,3-trifluoropropoxy, 3-iodobenzyloxy, isobutyl, isobutylamino, isobutoxy, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, isopropoxy, isopropyl, 4-isopropylbenzyloxy, 3-isopropylphenoxy, 4-isopropylphenoxy, isopropylthio, 4-isopropyl-3-methylphenoxy, 3-isothiazolyl, 4-isothiazolyl, 5-isothiazolyl, 3-methoxybenzyl, 4-methoxycarbonylbutoxy, 3-methoxycarbonylprop-2-enyloxy, 4-methoxyphenyl, 3-methoxyphenylamino, 4-methoxyphenylamino, 3-methylbenzyloxy, 4-methylbenzyloxy, 3-methylphenoxy, 3-methyl-4-methylthiophenoxy, 4-methylphenoxy, 1-methylpropoxy, 2-methylpyrid-5-yloxy, 4-methylthiophenoxy, 2-naphthyloxy, 2-nitrophenoxy, 4-nitrophenoxy, 3-nitrophenyl, 4-nitrophenylthio, 2-oxazolyl, 4-oxazolyl, 5-oxazolyl, pentafluoroethyl, pentafluoroethylthio, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, phenoxy, phenylamino, 1-phenylethoxy, phenylsulfonyl, 4-propanoylphenoxy, propoxy, 4-propylphenoxy, 4-propoxyphenoxy, thiophen-3-yl, *sec*-butyl, 4-*sec*-butylphenoxy,*tert* -butoxy, 3-*tert* -butylphenoxy, 4-*tert* -butylphenoxy, 1,1,2,2-tetrafluoroethoxy, tetrahydrofuran-2-yl, 2-(5,6,7,8-tetrahydronaphthyloxy), thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, thiophen-2-yl, 2,3,5-trifluorobenzyloxy, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, 3,3,3-trifluoro-2-hydroxypropyl, trifluoromethoxy, 3-trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, 3-trifluoromethoxyphenoxy, 4-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 4-trifluoromethylbenzyloxy, 2,4-bis-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl,

3-trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3-trifluoromethylphenyl, 3-trifluoromethylthiobenzyloxy, 4-trifluoromethylthiobenzyloxy, 2,3,4-trifluorophenoxy, 2,3,4-trifluorophenyl, 2,3,5-trifluorophenoxy, 3,4,5-trimethylphenoxy, 3-difluoromethoxyphenoxy, 3-pentafluoroethylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 3-trifluoromethylthiophenoxy, and trifluoromethylthio;

R_6 is selected from the group consisting of chloro, fluoro, hydrido, pentafluoroethyl, 1,1,2,2-tetrafluoroethoxy, trifluoromethyl, and trifluoromethoxy;

R_7 is selected from the group consisting of hydrido, fluoro, and trifluoromethyl.

In a more preferred specific embodiment of compounds of Formulas I-WOPA, I-WOHA, I-WOPC, and I-WOHC,

n is the integer 1;

R_1 is selected from the group consisting of trifluoromethyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, difluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

R_2 is selected from the group consisting of hydrido, methyl, ethyl, phenyl, 4-trifluoromethylphenyl, trifluoromethoxymethyl, 1,1,2,2-tetrafluoroethoxymethyl, difluoromethyl, pentafluoroethyl, trifluoromethyl, and 2,2,3,3,3-pentafluoropropyl;

R_3 is selected from the group consisting of hydrido, phenyl, 4-trifluoromethylphenyl, methyl, trifluoromethyl, difluoromethyl, and chlorodifluoromethyl;

Y and Z are independently selected from a covalent single bond and methylene;

R_4 and R_8 are independently selected from the group consisting of hydrido and fluoro;

R_5 is selected from the group consisting of benzyloxy, 5-bromo-2-fluorophenoxy, 4-bromo-3-fluorophenoxy, 3-bromobenzyloxy, 4-bromophenoxy, 4-butoxyphenoxy, 3-chlorobenzyloxy, 2-chlorophenoxy, 4-chloro-3-ethylphenoxy, 4-chloro-3-methylphenoxy, 2-chloro-4-fluorophenoxy, 4-chloro-2-fluorophenoxy, 4-chlorophenoxy, 3-chloro-4-ethylphenoxy, 3-chloro-4-methylphenoxy, 3-chloro-4-fluorophenoxy, 4-chloro-3-fluorophenoxy, 4-chlorophenylamino, 5-chloropyrid-3-yloxy, cyclobutoxy, cyclobutyl, cyclohexylmethoxy, cyclopentoxy, cyclopentyl, cyclopentylcarbonyl, cyclopropylmethoxy, 2,3-dichlorophenoxy, 2,4-dichlorophenoxy, 2,4-dichlorophenyl, 3,5-dichlorophenyl, 3,5-dichlorobenzyl, 3,4-dichlorophenoxy, 3,4-difluorophenoxy,2,3-difluorobenzyloxy, 3,5-difluorobenzyloxy, difluoromethoxy, 3,5-difluorophenoxy, 3,4-difluorophenyl, 2,3-difluorophenoxy, 2,4-difluorophenoxy, 2,5-difluorophenoxy, 3,5-dimethoxyphenoxy,3-dimethylaminophenoxy, 3,4-dimethylbenzyloxy, 3,5-dimethylbenzyloxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 1,3-dioxolan-2-yl, 3-ethylbenzyloxy, 3-ethylphenoxy, 4-ethylaminophenoxy, 3-ethyl-5-methylphenoxy, 4-fluoro-3-methylbenzyl, 4-fluorobenzyloxy, 2-fluoro-3-methylphenoxy, 3-fluoro-4-methylphenoxy, 3-fluorophenoxy, 3-fluoro-2-nitrophenoxy, 2-fluoro-3-trifluoromethylbenzyloxy, 3-fluoro-5-trifluoromethylbenzyloxy, 2-fluorophenoxy, 4-fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2-fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4-trifluoromethylphenoxy, 2-furyl, 3-furyl, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, 2-hydroxy-3,3,3-trifluoropropoxy, isobutoxy, isobutyl, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, isopropoxy, 3-isopropylbenzyloxy, 3-isopropylphenoxy, isopropylthio, 4-isopropyl-3-methylphenoxy, 3-isothiazolyl, 4-isothiazolyl, 5-isothiazolyl, 3-methoxybenzyl, 4-methoxyphenylamino, 3-methylbenzyloxy, 4-methylbenxyloxy, 3-methylphenoxy, 3-methyl-4-methylthiophenoxy, 4-methylphenoxy, 1-methylpropoxy, 2-methylpyrid-5-yloxy, 4-methylthiophenoxy, 2-naphthyloxy, 2-nitrophenoxy, 4-nitrophenoxy, 3-nitrophenyl, 2-oxazolyl, 4-oxazolyl, 5-oxazolyl, pentafluoroethyl, pentafluoroethylthio, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, phenoxy, phenylamino, 1-phenylethoxy,

4-propylphenoxy, 4-propoxyphenoxy, thiophen-3-yl,tert -butoxy, 3-tert -butylphenoxy, 4-tert -butylphenoxy, 1,1,2,2-tetrafluoroethoxy, tetrahydrofuran-2-yl, 2-(5,6,7,8-tetrahydronaphthyloxy), thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, thiophen-2-yl, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, 3,3,3-trifluoro-2-hydroxypropyl, trifluoromethoxy, 3-trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, 4-trifluoromethoxyphenoxy, 3-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, 3-trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3-trifluoromethylphenyl, 2,3,4-trifluorophenoxy, 2,3,5-trifluorophenoxy, 3,4,5-trimethylphenoxy, 3-difluoromethoxyphenoxy, 3-pentafluoroethylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 3-trifluoromethylthiophenoxy, 3-trifluoromethylthiobenzyloxy, and trifluoromethylthio;

R_6 is selected from the group consisting of chloro, fluoro, hydrido, pentafluoroethyl, 1,1,2,2-tetrafluoroethoxy, and trifluoromethyl;

R_7 is selected from the group consisting of hydrido, fluoro, and trifluoromethyl.

In an even more preferred specific embodiment of compounds of Formulas I-WOPA, I-WOHA, I-WOPC, and I-WOHC,

n is the integer 1;

R_1 is selected from the group consisting of trifluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

R_2 is hydrido, pentafluoroethyl, and trifluoromethyl;

R_3 is selected from the group consisting of hydrido, methyl, trifluoromethyl, and difluoromethyl

Y and Z are independently selected from the group consisting of a covalent single bond and methylene;

R_4 and R_8 are independently selected from the group consisting of hydrido and fluoro;

R_5 is selected from the group consisting of 5-bromo-2-fluorophenoxy, 4-chloro-3-ethylphenoxy, cyclopentyl, 2,3-dichlorophenoxy, 3,4-dichlorophenoxy, 3-difluoromethoxyphenoxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 3-ethylphenoxy, 3-ethyl-5-methylphenoxy, 4-fluoro-3-methylphenoxy, 4-fluorophenoxy, 2-furyl, isobutyl, isopropoxy, 3-isopropylphenoxy, 3-methylphenoxy, pentafluoroethyl, 3-pentafluoroethylphenoxy, 3-tert -butylphenoxy, 1,1,2,2-tetrafluoroethoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 2-(5,6,7,8-tetrahydronaphthyloxy), trifluoromethoxy, 3-trifluoromethoxybenzyloxy,3-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, trifluoromethylthio, and 3-trifluoromethylthiophenoxy;

R_6 is selected from the group consisting of fluoro and hydrido;

R_7 is selected from the group consisting of hydrido and fluoro.

In a preferred specific embodiment of compounds of Formulas I-WOPA and I-WOHA,

A is selected from the group consisting of ethyl, 1-propenyl, propyl, isopropyl, butyl, 2-butenyl, 3-butenyl, 2-butynyl, *sec*-butyl, isobutyl, 2-methylpropenyl, 1-pentyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, 2-pentynyl, 3-pentynyl, 2-pentyl, 1-methyl-2-butenyl, 1-methyl-3-butenyl, 1-methyl-2-butynyl, 3-pentyl, 1-ethyl-2-propenyl, 2-methylbutyl, 2-methyl-2-butenyl, 2-methyl-3-butenyl, 2-methyl-3-butynyl, 3-methylbutyl, 3-methyl-2-butenyl, 3-methyl-3-butenyl, 1-hexyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, 5-hexenyl, 2-hexynyl, 3-hexynyl, 4-hexynyl, 2-hexyl, 1-methyl-2-pentenyl, 1-methyl-3-pentenyl, 1-methyl-4-pentenyl, 1-methyl-2-pentynyl, 1-methyl-3-pentynyl, 3-hexyl, 1-ethyl-2-butenyl, 1-ethyl-3-butenyl, 1-propyl-2-propenyl, 1-ethyl-2-butynyl, 1-heptyl, 2-heptenyl, 3-heptenyl, 4-heptenyl, 5-heptenyl, 6-heptenyl, 2-heptynyl, 3-heptynyl, 4-heptynyl, 5-heptynyl, 2-heptyl, 1-methyl-2-hexenyl, 1-methyl-3-hexenyl, 1-methyl-4-hexenyl, 1-methyl-5-hexenyl, 1-methyl-2-hexynyl, 1-methyl-3-hexynyl, 1-methyl-4-hexynyl, 3-heptyl, 1-ethyl-2-pentenyl, 1-ethyl-3-pentenyl, 1-ethyl-4-pentenyl, 1-butyl-2-propenyl, 1-ethyl-2-pentynyl, 1-ethyl-3-pentynyl, 1-octyl, 2-octenyl, 3-octenyl, 4-octenyl, 5-octenyl, 6-octenyl, 7-octenyl, 2-octynyl, 3-octynyl, 4-octynyl, 5-octynyl, 6-octynyl, 2-octyl, 1-methyl-2-heptenyl, 1-methyl-3-heptenyl, 1-methyl-4-

heptenyl, 1-methyl-5-heptenyl, 1-methyl-6-heptenyl, 1-methyl-2-heptynyl, 1-methyl-3-heptynyl, 1-methyl-4-heptenyl, 1-methyl-5-heptenyl, 1-methyl-6-heptenyl, 1-methyl-2-heptenyl, 1-methyl-3-heptynyl, 1-methyl-4-heptynyl, 1-methyl-5-heptynyl, 3-octyl, 1-ethyl-2-hexenyl, 1-ethyl-3-hexenyl, 1-ethyl-4-hexenyl, 1-ethyl-2-hexynyl, 1-ethyl-3-hexynyl, 1-ethyl-4-hexynyl, 1-ethyl-5-hexenyl, 1-pentyl-2-propenyl, 4-octyl, 1-propyl-2-pentenyl, 1-propyl-3-pentenyl, 1-propyl-4-pentenyl, 1-butyl-2-butenyl, 1-propyl-2-pentynyl, 1-propyl-3-pentynyl, 1-butyl-2-butynyl, 1-butyl-3-butenyl, 2,2-difluoropropyl, 4-trifluoromethyl-5,5,5-trifluoropentyl, 4-trifluoromethylpentyl, 5,5,6,6,6-pentafluorohexyl, 3,3,3-trifluoropropyl, 2-methoxyethyl, 2-ethoxyethyl, 2-propoxyethyl, 2-isopropoxyethyl, 2-butoxyethyl, 2-isobutoxyethyl, 2-*sec*-butoxyethyl, 2-pentoxyethyl, 2-hexoxyethyl, 3-methoxypropyl, 2-methoxyisopropyl, 3-ethoxypropyl, 2-ethoxyisopropyl, 3-propoxypropyl, 2-propoxyisopropyl, 3-isopropoxypropyl, 2-isopropoxyisopropyl, 3-butoxypropyl, 2-butoxyisopropyl, 3-isobutoxypropyl, 2-isobutoxyisopropyl, 3-pentoxypropyl, and 2-pentoxyisopropyl, wherein each member of group A may be optionally substituted at any carbon up to and including 6 atoms from the point of attachment of A to Z with one or more of the group consisting of R_{33}, R_{34}, R_{35}, and R_{36} with the provisos that R_{33}, R_{34}, R_{35}, and R_{36} must not be attached to the carbon directly linking A to Z and that R_{33}, R_{34}, R_{35}, and R_{36} must be selected from other than aryl and heteroaryl when substituting the carbon 2 atoms from Z wherein Z is a single covalent bond;

R_{33}, R_{34}, R_{35}, and R_{36} are independently selected from the group consisting of cyano, hydroxy, 4-aminophenoxy, benzoyl, benzyl, benzyloxy, 5-bromo-2-fluorophenoxy, 4-bromo-3-fluorophenoxy, 4-bromo-2-nitrophenoxy, 3-bromobenzyloxy, 4-bromobenzyloxy, 4-bromophenoxy, 5-bromopyrid-2-yloxy, 4-butoxyphenoxy, chloro, 3-chlorobenzyl, 2-chlorophenoxy, 4-chlorophenoxy, 4-chloro-3-ethylphenoxy, 3-chloro-4-fluorobenzyl, 3-chloro-4-fluorophenyl, 3-chloro-2-fluorobenzyloxy, 3-chlorobenzyloxy, 4-chlorobenzyloxy, 4-chloro-3-methylphenoxy, 2-chloro-4-fluorophenoxy, 4-chloro-2-fluorophenoxy, 4-chlorophenoxy, 3-chloro-4-ethylphenoxy, 3-chloro-4-methylphenoxy, 3-chloro-4-fluorophenoxy,

4-chloro-3-fluorophenoxy, 4-chlorophenylamino, 5-chloropyrid-3-yloxy, 2-cyanopyrid-3-yloxy, 4-cyanophenoxy, cyclobutoxy, cyclobutyl, cyclohexoxy, cyclohexylmethoxy, cyclopentoxy, cyclopentyl, cyclopentylcarbonyl, cyclopropyl, cyclopropylmethoxy, cyclopropoxy, 2,3-dichlorophenoxy, 2,4-dichlorophenoxy, 2,4-dichlorophenyl, 3,5-dichlorophenyl, 3,5-dichlorobenzyl, 3,4-dichlorophenoxy, 3,4-difluorophenoxy, 2,3-difluorobenzyloxy, 2,4-difluorobenzyloxy, 3,4-difluorobenzyloxy, 2,5-difluorobenzyloxy, 3,5-difluorophenoxy, 3,4-difluorophenyl, 3,5-difluorobenzyloxy, 4-difluoromethoxybenzyloxy, 2,3-difluorophenoxy, 2,4-difluorophenoxy, 2,5-difluorophenoxy, 3,5-dimethoxyphenoxy, 3-dimethylaminophenoxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 3,4-dimethylbenzyl, 3,4-dimethylbenzyloxy, 3,5-dimethylbenzyloxy, 2,2-dimethylpropoxy, 1,3-dioxan-2-yl, 1,4-dioxan-2-yl, 1,3-dioxolan-2-yl, ethoxy, 4-ethoxyphenoxy, 4-ethylbenzyloxy, 3-ethylphenoxy, 4-ethylaminophenoxy, 3-ethyl-5-methylphenoxy, fluoro, 4-fluoro-3-methylbenzyl, 4-fluoro-3-methylphenyl, 4-fluoro-3-methylbenzoyl, 4-fluorobenzyloxy, 2-fluoro-3-methylphenoxy, 3-fluoro-4-methylphenoxy, 3-fluorophenoxy, 3-fluoro-2-nitrophenoxy, 2-fluoro-3-trifluoromethylbenzyloxy, 3-fluoro-5-trifluoromethylbenzyloxy, 4-fluoro-2-trifluoromethylbenzyloxy, 4-fluoro-3-trifluoromethylbenzyloxy, 2-fluorophenoxy, 4-fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2-fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4-trifluoromethylphenoxy, 4-fluoropyrid-2-yloxy, 2-furyl, 3-furyl, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, 2-hydroxy-3,3,3-trifluoropropoxy, 3-iodobenzyloxy, isobutyl, isobutylamino, isobutoxy, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, isopropoxy, isopropyl, 4-isopropylbenzyloxy, 3-isopropylphenoxy, 4-isopropylphenoxy, isopropylthio, 4-isopropyl-3-methylphenoxy, 3-isothiazolyl, 4-isothiazolyl, 5-isothiazolyl, 3-methoxybenzyl, 4-methoxycarbonylbutoxy, 3-methoxycarbonylprop-2-enyloxy, 4-methoxyphenyl, 3-methoxyphenylamino, 4-methoxyphenylamino, 3-methylbenzyloxy, 4-methylbenzyloxy, 3-methylphenoxy, 3-methyl-4-methylthiophenoxy, 4-methylphenoxy, 1-methylpropoxy, 2-methylpyrid-5-yloxy, 4-methylthiophenoxy, 2-naphthyloxy, 2-nitrophenoxy, 4-nitrophenoxy,

3-nitrophenyl, 4-nitrophenylthio, 2-oxazolyl, 4-oxazolyl, 5-oxazolyl, pentafluoroethyl, pentafluoroethylthio, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, phenoxy, phenylamino, 1-phenylethoxy, phenylsulfonyl, 4-propanoylphenoxy, propoxy, 4-propylphenoxy, 4-propoxyphenoxy, thiophen-3-yl, *sec*-butyl, 4-*sec*-butylphenoxy,*tert*-butoxy, 3-*tert*-butylphenoxy, 4-*tert*-butylphenoxy, 1,1,2,2-tetrafluoroethoxy, tetrahydrofuran-2-yl, 2-(5,6,7,8-tetrahydronaphthyloxy), thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, thiophen-2-yl, 2,3,5-trifluorobenzyloxy, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, 3,3,3-trifluoro-2-hydroxypropyl, trifluoromethoxy, 3-trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, 3-trifluoromethoxyphenoxy, 4-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 4-trifluoromethylbenzyloxy, 2,4-bis-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, 3-trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3-trifluoromethylphenyl, 3-trifluoromethylthiobenzyloxy, 4-trifluoromethylthiobenzyloxy, 2,3,4-trifluorophenoxy, 2,3,4-trifluorophenyl, 2,3,5-trifluorophenoxy, 3,4,5-trimethylphenoxy, 3-difluoromethoxyphenoxy, 3-pentafluoroethylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 3-trifluoromethylthiophenoxy, and trifluoromethylthio.

In a preferred specific embodiment of compounds of Formulas I-WOPA and I-WOHA,

A is selected from the group consisting of ethyl, 1-propenyl, propyl, isopropyl, butyl, 2-butenyl, 3-butenyl, *sec*-butyl, isobutyl, 2-methylpropenyl, 1-pentyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, 2-pentyl, 1-methyl-2-butenyl, 1-methyl-3-butenyl, 3-pentyl, 1-ethyl-2-propenyl, 2-methylbutyl, 2-methyl-2-butenyl, 2-methyl-3-butenyl, 3-methylbutyl, 3-methyl-2-butenyl, 3-methyl-3-butenyl, 1-hexyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, 5-hexenyl, 2-hexyl, 1-methyl-2-pentenyl, 1-methyl-3-pentenyl, 1-methyl-4-pentenyl, 3-hexyl, 1-ethyl-2-butenyl, 1-ethyl-3-butenyl, 1-propyl-2-propenyl, 1-heptyl, 2-heptenyl, 3-heptenyl, 4-heptenyl, 5-heptenyl, 6-heptenyl, 2-heptyl, 1-methyl-2-hexenyl, 1-methyl-3-hexenyl, 1-methyl-4-hexenyl, 1-methyl-5-hexenyl, 3-heptyl, 1-ethyl-2-pentenyl, 1-ethyl-3-pentenyl, 1-ethyl-4-pentenyl, 1-butyl-2-propenyl,

1-octyl, 2-octenyl, 3-octenyl, 4-octenyl, 5-octenyl, 6-octenyl, 7-octenyl, 2-octyl, 1-methyl-2-heptenyl, 1-methyl-3-heptenyl, 1-methyl-4-heptenyl, 1-methyl-5-heptenyl, 1-methyl-6-heptenyl, 1-methyl-4-heptenyl, 1-methyl-6-heptenyl, 1-methyl-2-heptenyl, 3-octyl, 1-ethyl-2-hexenyl, 1-ethyl-3-hexenyl, 1-ethyl-4-hexenyl, 1-ethyl-5-hexenyl, 1-pentyl-2-propenyl, 4-octyl, 1-propyl-2-pentenyl, 1-propyl-3-pentenyl, 1-propyl-4-pentenyl, 1-butyl-2-butenyl, 1-butyl-3-butenyl, 2,2-difluoropropyl, 4-trifluoromethyl-5,5,5-trifluoropentyl, 4-trifluoromethylpentyl, 5,5,6,6,6-pentafluorohexyl, and 3,3,3-trifluoropropyl, wherein each member of group A may be optionally substituted at any carbon up to and including 6 atoms from the point of attachment of A to Z with one or more of the group consisting of R_{33}, R_{34}, R_{35}, and R_{36} with the provisos that R_{33}, R_{34}, R_{35}, and R_{36} must not be attached to the carbon directly linking A to Z and that R_{33}, R_{34}, R_{35}, and R_{36} must be selected from other than aryl and heteroaryl when substituting the carbon 2 atoms from Z wherein Z is a single covalent bond;

R_{33}, R_{34}, R_{35}, and R_{36} are independently selected from the group consisting of benzyloxy, 5-bromo-2-fluorophenoxy, 4-bromo-3-fluorophenoxy, 3-bromobenzyloxy, 4-bromophenoxy,4-butoxyphenoxy, 3-chlorobenzyloxy, 2-chlorophenoxy, 4-chloro-3-ethylphenoxy, 4-chloro-3-methylphenoxy, 2-chloro-4-fluorophenoxy, 4-chloro-2-fluorophenoxy, 4-chlorophenoxy, 3-chloro-4-ethylphenoxy, 3-chloro-4-methylphenoxy, 3-chloro-4-fluorophenoxy, 4-chloro-3-fluorophenoxy, 4-chlorophenylamino, 5-chloropyrid-3-yloxy, cyclobutoxy, cyclobutyl, cyclohexylmethoxy, cyclopentoxy, cyclopentyl, cyclopentylcarbonyl, cyclopropylmethoxy, 2,3-dichlorophenoxy, 2,4-dichlorophenoxy, 2,4-dichlorophenyl, 3,5-dichlorophenyl, 3,5-dichlorobenzyl, 3,4-dichlorophenoxy, 3,4-difluorophenoxy,2,3-difluorobenzyloxy, 3,5-difluorobenzyloxy, difluoromethoxy, 3,5-difluorophenoxy, 3,4-difluorophenyl, 2,3-difluorophenoxy, 2,4-difluorophenoxy, 2,5-difluorophenoxy, 3,5-dimethoxyphenoxy,3-dimethylaminophenoxy, 3,4-dimethylbenzyloxy, 3,5-dimethylbenzyloxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 1,3-dioxolan-2-yl, 3-ethylbenzyloxy, 3-ethylphenoxy, 4-ethylaminophenoxy,

3-ethyl-5-methylphenoxy, 4-fluoro-3-methylbenzyl, 4-fluorobenzyloxy, 2-fluoro-3-methylphenoxy, 3-fluoro-4-methylphenoxy, 3-fluorophenoxy, 3-fluoro-2-nitrophenoxy, 2-fluoro-3-trifluoromethylbenzyloxy, 3-fluoro-5-trifluoromethylbenzyloxy, 2-fluorophenoxy, 4-fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2-fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4-trifluoromethylphenoxy, 2-furyl, 3-furyl, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, 2-hydroxy-3,3,3-trifluoropropoxy, isobutoxy, isobutyl, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, isopropoxy, 3-isopropylbenzyloxy, 3-isopropylphenoxy, isopropylthio, 4-isopropyl-3-methylphenoxy, 3-isothiazolyl, 4-isothiazolyl, 5-isothiazolyl, 3-methoxybenzyl, 4-methoxyphenylamino, 3-methylbenzyloxy, 4-methylbenxyloxy, 3-methylphenoxy, 3-methyl-4-methylthiophenoxy, 4-methylphenoxy, 1-methylpropoxy, 2-methylpyrid-5-yloxy, 4-methylthiophenoxy, 2-naphthyloxy, 2-nitrophenoxy, 4-nitrophenoxy, 3-nitrophenyl, 2-oxazolyl, 4-oxazolyl, 5-oxazolyl, pentafluoroethyl, pentafluoroethylthio, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, phenoxy, phenylamino, 1-phenylethoxy, 4-propylphenoxy, 4-propoxyphenoxy, thiophen-3-yl,tert -butoxy, 3-tert -butylphenoxy, 4-tert -butylphenoxy, 1,1,2,2-tetrafluoroethoxy, tetrahydrofuran-2-yl, 2-(5,6,7,8-tetrahydronaphthyloxy), thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, thiophen-2-yl, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, 3,3,3-trifluoro-2-hydroxypropyl, trifluoromethoxy, 3-trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, 4-trifluoromethoxyphenoxy, 3-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, 3-trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3-trifluoromethylphenyl, 2,3,4-trifluorophenoxy, 2,3,5-trifluorophenoxy, 3,4,5-trimethylphenoxy, 3-difluoromethoxyphenoxy, 3-pentafluoroethylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 3-trifluoromethylthiophenoxy, 3-trifluoromethylthiobenzyloxy, and trifluoromethylthio.

In an even more preferred specific embodiment of compounds of Formulas I-WOPA and I-WOHA.

A is selected from the group consisting of 1-propenyl, propyl, isopropyl, butyl, 2-butenyl, 3-butenyl, *sec*-butyl, isobutyl, 2-methylpropenyl, 1-pentyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, 2-pentyl, 1-methyl-2-butenyl, 1-methyl-3-butenyl, 3-pentyl, 1-ethyl-2-propenyl, 2-methylbutyl, 2-methyl-2-butenyl, 2-methyl-3-butenyl, 3-methylbutyl, 3-methyl-2-butenyl, 3-methyl-3-butenyl, 1-hexyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, 5-hexenyl, 2-hexyl, 1-methyl-2-pentenyl, 1-methyl-3-pentenyl, 1-methyl-4-pentenyl, 3-hexyl, 1-ethyl-2-butenyl, 1-ethyl-3-butenyl, 1-propyl-2-propenyl, 1-ethyl-2-pentenyl, 1-ethyl-3-pentenyl, 1-ethyl-4-pentenyl, 1-butyl-2-propenyl, 1-ethyl-2-hexenyl, 1-ethyl-3-hexenyl, 1-ethyl-4-hexenyl, 1-ethyl-5-hexenyl, 1-pentyl-2-propenyl,1-propyl-2-pentenyl, 1-propyl-3-pentenyl, 1-propyl-4-pentenyl, 1-butyl-2-butenyl, 1-butyl-3-butenyl, 2,2-difluoropropyl, 4-trifluoromethyl-5,5,5-trifluoropentyl, 4-trifluoromethylpentyl, 5,5,6,6,6-pentafluorohexyl, and 3,3,3-trifluoropropyl, wherein each member of group A may be optionally substituted at any carbon up to and including 6 atoms from the point of attachment of A to Z with one or more of the group consisting of R_{33}, R_{34}, R_{35}, and R_{36} with the provisos that R_{33}, R_{34}, R_{35}, and R_{36} must not be attached to the carbon directly linking A to Z and that R_{33}, R_{34}, R_{35}, and R_{36} must be selected from other than aryl and heteroaryl when substituting the carbon 2 atoms from Z wherein Z is a single covalent bond;

R_{33}, R_{34}, R_{35}, and R_{36} are independently selected from the group consisting of 5-bromo-2-fluorophenoxy, 4-chloro-3-ethylphenoxy, cyclopentyl, 2,3-dichlorophenoxy, 3,4-dichlorophenoxy, 3-difluoromethoxyphenoxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 3-ethylphenoxy, 3-ethyl-5-methylphenoxy, 4-fluoro-3-methylphenoxy, 4-fluorophenoxy, 2-furyl, isobutyl, isopropoxy, 3-isopropylphenoxy, 3-methylphenoxy, pentafluoroethyl, 3-pentafluoroethylphenoxy, 3-tert -butylphenoxy, 1,1,2,2-tetrafluoroethoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 2-(5,6,7,8-tetrahydronaphthyloxy),trifluoromethoxy, 3-trifluoromethoxybenzyloxy,3-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, trifluoromethylthio, and 3-trifluoromethylthiophenoxy.

In a preferred specific embodiment of compounds of Formulas I-WOHA and I-WOHC,

D_1, D_2, J_1, J_2 and K_1 are independently selected from the group consisting of C, N, O, S and a covalent bond to form the group consisting of 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrrolyl, 3-pyrrolyl, 2-imidazolyl, 4-imidazolyl, 3-pyrazolyl, 4-pyrazolyl, 1,2,4-triazol-3-yl, 1,2,4-triazol-5-yl, 1,2,4-oxadiazol-3-yl, 1,2,4-oxadiazol-5-yl, 1,3,4-oxadiazol-3-yl, 1,3,4-oxadiazol-5-yl, 3-isothiazolyl, 5-isothiazolyl, 2-oxazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl, 4-pyridazinyl, 1,3,5-triazin-2-yl, 1,2,4-triazin-3-yl, 1,2,4-triazin-5-yl, 1,2,4-triazin-6-yl, 1,2,3-triazin-4-yl, 1-indolizinyl, 7-indolizinyl, 1-isoquinolyl, and 2-quinolyl, wherein a ring carbon atom adjacent to the carbon atom at the point of attachment may be optionally substituted with R_4 or R_8, a ring carbon atom adjacent to the R_4 position and two atoms from the point of attachment may be substituted with R5, a ring carbon atom adjacent to the R_8 position and two atoms from the point of attachment may be substituted with R_7, and a ring carbon atom three atoms from the point of attachment and adjacent to the R_5 and R_7 positions may be substituted with R_6.

In a more preferred specific embodiment of compounds of Formulas I-WOHA and I-WOHC,

D_1, D_2, J_1, J_2 and K_1 are independently selected from the group consisting of C, N, O, S and a covalent bond to form the group consisting of 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrrolyl, 3-pyrrolyl, 2-imidazolyl, 4-imidazolyl, 3-pyrazolyl, 4-pyrazolyl, 2-oxazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl, 4-pyridazinyl, 1,3,5-triazin-2-yl, 1-indolizinyl, 7-indolizinyl, 1-isoquinolyl, and 2-quinolyl, wherein a ring carbon atom adjacent to the carbon atom at the point of attachment may be optionally

substituted with R_4 or R_8, a ring carbon atom adjacent to the R_4 position and two atoms from the point of attachment may be substituted with R5, a ring carbon atom adjacent to the R_8 position and two atoms from the point of attachment may be substituted with R_7, and a ring carbon atom three atoms from the point of attachment and adjacent to the R_5 and R_7 positions may be substituted with R_6.

In an even more preferred specific embodiment of compounds of Formulas I-WOHA and I-WOHC,

D_1, D_2, J_1, J_2 and K_1 are independently selected from the group consisting of C, N, O, S and a covalent bond to form the group consisting of 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrrolyl, 3-pyrrolyl, 2-imidazolyl, 4-imidazolyl, 3-pyrazolyl, 4-pyrazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl, 4-pyridazinyl, and 1,3,5-triazin-2-yl, wherein a ring carbon atom adjacent to the carbon atom at the point of attachment may be optionally substituted with R_4 or R_8, a ring carbon atom adjacent to the R_4 position and two atoms from the point of attachment may be substituted with R5, a ring carbon atom adjacent to the R_8 position and two atoms from the point of attachment may be substituted with R_7, and a ring carbon atom three atoms from the point of attachment and adjacent to the R_5 and R_7 positions may be substituted with R_6.

In a preferred specific embodiment of compounds of Formulas I-WOPC and I-WOHC,

A is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclopent-2-enyl, cyclopent-3-enyl, cyclohexyl, 4-methylcyclohexyl, 4-chloro-3-ethylphenoxycyclohexyl, 3-

trifluoromethoxyphenoxycyclohexyl, 3-trifluoromethylcyclohexyl, 4-trifluoromethylcyclohexyl, 3,5-bis-trifluoromethylcyclohexyl, adamantyl, 3-trifluoromethyladamantyl, norbornyl, 3-trifluoromethylnorbornyl, norbornenyl, 7-oxabicyclo[2.2.1]heptan-2-yl, bicyclo[3.1.0]hexan-6-yl, cyclohex-2-enyl, cyclohex-3-enyl, cycloheptyl, cyclohept-2-enyl, cyclohept-3-enyl, cyclooctyl, cyclooct-2-enyl, cyclooct-3-enyl, cyclooct-4-enyl, 2-morpholinyl, 3-morpholinyl, 4-morpholinyl, 1-piperazinyl, 2-piperazinyl, 1-piperidinyl, 2-piperidinyl, 3-piperidinyl, 4-piperidinyl, 1-pyrrolidinyl, 2-pyrrolidinyl, 3-pyrrolidinyl, 2-dioxanyl, 2H-2-pyranyl, 2H-3-pyranyl, 2H-4-pyranyl, 4H-2-pyranyl, 4H-3-pyranyl, 4H-4-pyranyl, 2H-pyran-2-one-3-yl, 2H-pyran-2-one-4-yl, 2H-pyran-2-one-5-yl, 4H-pyran-4-one-2-yl, 4H-pyran-4-one-3-yl, 2-tetrahydrofuranyl, 3-tetrahydrofuranyl, 2-tetrahydropyranyl, 3-tetrahydropyranyl, 4-tetrahydropyranyl, 2-tetrahydrothienyl, and 3-tetrahydrothienyl, wherein each ring carbon may be optionally substituted with R_{30}, a ring carbon other than the ring carbon at the point of attachment of A to Z may be optionally substituted with oxo provided that no more than one ring carbon is substituted by oxo at the same time, ring carbon and nitrogen atoms adjacent to the carbon atom at the point of attachment may be optionally substituted with R_9 or R_{13}, a ring carbon or nitrogen atom adjacent to the R_9 position and two atoms from the point of attachment may be substituted with R_{10}, a ring carbon or nitrogen atom adjacent to the R_{13} position and two atoms from the point of attachment may be substituted with R_{12}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{10} position may be substituted with R_{11}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{12} position may be substituted with R_{32}, and a ring carbon or nitrogen atom four atoms from the point of attachment and adjacent to the R_{11} and R_{32} positions may be substituted with R_{31};

R_9 and R_{13} are fluoro;

R_{10} and R_{12} are independently selected from the group consisting of 4-aminophenoxy, benzoyl, benzyl, benzyloxy, 5-bromo-2-fluorophenoxy, 4-bromo-3-fluorophenoxy, 4-bromo-2-nitrophenoxy, 3-bromobenzyloxy, 4-bromobenzyloxy, 4-bromophenoxy, 5-bromopyrid-2-yloxy, 4-butoxyphenoxy, chloro, 3-chlorobenzyl, 2-chlorophenoxy, 4-chlorophenoxy, 4-chloro-3-ethylphenoxy, 3-chloro-4-fluorobenzyl, 3-chloro-4-fluorophenyl, 3-chloro-2-fluorobenzyloxy, 3-chlorobenzyloxy, 4-chlorobenzyloxy, 4-chloro-3-methylphenoxy, 2-chloro-4-fluorophenoxy, 4-chloro-2-fluorophenoxy, 4-chlorophenoxy, 3-chloro-4-ethylphenoxy, 3-chloro-4-methylphenoxy, 3-chloro-4-fluorophenoxy, 4-chloro-3-fluorophenoxy, 4-chlorophenylamino, 5-chloropyrid-3-yloxy, 2-cyanopyrid-3-yloxy, 4-cyanophenoxy, cyclobutoxy, cyclobutyl, cyclohexoxy, cyclohexylmethoxy, cyclopentoxy, cyclopentyl, cyclopentylcarbonyl, cyclopropyl, cyclopropylmethoxy, cyclopropoxy, 2,3-dichlorophenoxy, 2,4-dichlorophenoxy, 2,4-dichlorophenyl, 3,5-dichlorophenyl, 3,5-dichlorobenzyl, 3,4-dichlorophenoxy, 3,4-difluorophenoxy, 2,3-difluorobenzyloxy, 2,4-difluorobenzyloxy, 3,4-difluorobenzyloxy, 2,5-difluorobenzyloxy, 3,5-difluorophenoxy, 3,4-difluorophenyl, 3,5-difluorobenzyloxy, 4-difluoromethoxybenzyloxy, 2,3-difluorophenoxy, 2,4-difluorophenoxy, 2,5-difluorophenoxy, 3,5-dimethoxyphenoxy, 3-dimethylaminophenoxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 3,4-dimethylbenzyl, 3,4-dimethylbenzyloxy, 3,5-dimethylbenzyloxy, 2,2-dimethylpropoxy, 1,3-dioxan-2-yl, 1,4-dioxan-2-yl, 1,3-dioxolan-2-yl, ethoxy, 4-ethoxyphenoxy, 4-ethylbenzyloxy, 3-ethylphenoxy, 4-ethylaminophenoxy, 3-ethyl-5-methylphenoxy, fluoro, 4-fluoro-3-methylbenzyl, 4-fluoro-3-methylphenyl, 4-fluoro-3-methylbenzoyl, 4-fluorobenzyloxy, 2-fluoro-3-methylphenoxy, 3-fluoro-4-methylphenoxy, 3-fluorophenoxy, 3-fluoro-2-nitrophenoxy, 2-fluoro-3-trifluoromethylbenzyloxy, 3-fluoro-5-trifluoromethylbenzyloxy, 4-fluoro-2-trifluoromethylbenzyloxy, 4-fluoro-3-trifluoromethylbenzyloxy, 2-fluorophenoxy, 4-fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2-fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4-trifluoromethylphenoxy, 4-fluoropyrid-2-yloxy, 2-furyl, 3-furyl, heptafluoropropyl,

1,1,1,3,3,3-hexafluoropropyl, 2-hydroxy-3,3,3-trifluoropropoxy, 3-iodobenzyloxy, isobutyl, isobutylamino, isobutoxy, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, isopropoxy, isopropyl, 4-isopropylbenzyloxy, 3-isopropylphenoxy, 4-isopropylphenoxy, isopropylthio, 4-isopropyl-3-methylphenoxy, 3-isothiazolyl, 4-isothiazolyl, 5-isothiazolyl, 3-methoxybenzyl, 4-methoxycarbonylbutoxy, 3-methoxycarbonylprop-2-enyloxy, 4-methoxyphenyl, 3-methoxyphenylamino, 4-methoxyphenylamino, 3-methylbenzyloxy, 4-methylbenzyloxy, 3-methylphenoxy, 3-methyl-4-methylthiophenoxy, 4-methylphenoxy, 1-methylpropoxy, 2-methylpyrid-5-yloxy, 4-methylthiophenoxy, 2-naphthyloxy, 2-nitrophenoxy, 4-nitrophenoxy, 3-nitrophenyl, 4-nitrophenylthio, 2-oxazolyl, 4-oxazolyl, 5-oxazolyl, pentafluoroethyl, pentafluoroethylthio, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, phenoxy, phenylamino, 1-phenylethoxy, phenylsulfonyl, 4-propanoylphenoxy, propoxy, 4-propylphenoxy, 4-propoxyphenoxy, thiophen-3-yl, *sec*-butyl, 4-*sec*-butylphenoxy,*tert*-butoxy, 3-*tert*-butylphenoxy, 4-*tert*-butylphenoxy, 1,1,2,2-tetrafluoroethoxy, tetrahydrofuran-2-yl, 2-(5,6,7,8-tetrahydronaphthyloxy), thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, thiophen-2-yl, 2,3,5-trifluorobenzyloxy, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, 3,3,3-trifluoro-2-hydroxypropyl, trifluoromethoxy, 3-trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, 3-trifluoromethoxyphenoxy, 4-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 4-trifluoromethylbenzyloxy, 2,4-bis-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, 3-trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3-trifluoromethylphenyl, 3-trifluoromethylthiobenzyloxy, 4-trifluoromethylthiobenzyloxy, 2,3,4-trifluorophenoxy, 2,3,4-trifluorophenyl, 2,3,5-trifluorophenoxy, 3,4,5-trimethylphenoxy, 3-difluoromethoxyphenoxy, 3-pentafluoroethylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 3-trifluoromethylthiophenoxy, and trifluoromethylthio;

R_{11}, R_{31}, and R_{32} are independently selected from the group consisting of chloro, fluoro, hydrido, pentafluoroethyl, 1,1,2,2-tetrafluoroethoxy, trifluoromethyl, and trifluoromethoxy;

R_{30} is selected from the group consisting of chloro, ethoxy, ethyl, fluoro, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, isobutyl, isobutoxy, isopropoxy, isopropyl, isopropylthio, methyl, propyl, pentafluoroethyl, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, propoxy, *sec*-butyl, *tert*-butoxy, 1,1,2,2-tetrafluoroethoxy, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, trifluoromethoxy, and trifluoromethyl.

In a more preferred specific embodiment of compounds of Formulas I-WOPC and I-WOHC,

A is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 4-methylcyclohexyl, 4-chloro-3-ethylphenoxycyclohexyl, 3-trifluoromethoxyphenoxycyclohexyl, 3-trifluoromethylcyclohexyl, 4-trifluoromethylcyclohexyl, 3,5-bis-trifluoromethylcyclohexyl, adamantyl, 3-trifluoromethyladamantyl, norbornyl, 3-trifluoromethylnorbornyl, norbornenyl, 7-oxabicyclo[2.2.1]heptan-2-yl, bicyclo[3.1.0]hexan-6-yl, cycloheptyl, cyclooctyl, 2-morpholinyl, 3-morpholinyl, 4-morpholinyl, 1-piperazinyl, 2-piperazinyl, 1-piperidinyl, 2-piperidinyl, 3-piperidinyl, 4-piperidinyl, 1-pyrrolidinyl, 2-pyrrolidinyl, 3-pyrrolidinyl, 2-dioxanyl, 4H-2-pyranyl, 4H-3-pyranyl, 4H-4-pyranyl, 4H-pyran-4-one-2-yl, 4H-pyran-4-one-3-yl, 2-tetrahydrofuranyl, 3-tetrahydrofuranyl, 2-tetrahydropyranyl, 3-tetrahydropyranyl, 4-tetrahydropyranyl, 2-tetrahydrothienyl, and 3-tetrahydrothienyl, wherein each ring carbon may be optionally substituted with R_{30}, a ring carbon other than the ring carbon at the point of attachment of A to Z may be optionally substituted with oxo provided that no more than one ring carbon is substituted by oxo at the same time, ring carbon and nitrogen atoms adjacent to the carbon atom at the point of attachment may be optionally substituted with R_9 or R_{13}, a ring carbon or nitrogen atom adjacent to the R_9 position and two atoms from

the point of attachment may be substituted with R_{10}, a ring carbon or nitrogen atom adjacent to the R_{13} position and two atoms from the point of attachment may be substituted with R_{12}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{10} position may be substituted with R_{11}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{12} position may be substituted with R_{32}, and a ring carbon or nitrogen atom four atoms from the point of attachment and adjacent to the R_{11} and R_{32} positions may be substituted with R_{31};

R_9 and R_{13} are fluoro;

R_{10} and R_{12} are independently selected from the group consisting of benzyloxy, 5-bromo-2-fluorophenoxy, 4-bromo-3-fluorophenoxy, 3-bromobenzyloxy, 4-bromophenoxy,4-butoxyphenoxy, 3-chlorobenzyloxy, 2-chlorophenoxy, 4-chloro-3-ethylphenoxy, 4-chloro-3-methylphenoxy, 2-chloro-4-fluorophenoxy, 4-chloro-2-fluorophenoxy, 4-chlorophenoxy, 3-chloro-4-ethylphenoxy, 3-chloro-4-methylphenoxy, 3-chloro-4-fluorophenoxy, 4-chloro-3-fluorophenoxy, 4-chlorophenylamino, 5-chloropyrid-3-yloxy, cyclobutoxy, cyclobutyl, cyclohexylmethoxy, cyclopentoxy, cyclopentyl, cyclopentylcarbonyl, cyclopropylmethoxy, 2,3-dichlorophenoxy, 2,4-dichlorophenoxy, 2,4-dichlorophenyl, 3,5-dichlorophenyl, 3,5-dichlorobenzyl, 3,4-dichlorophenoxy, 3,4-difluorophenoxy,2,3-difluorobenzyloxy, 3,5-difluorobenzyloxy, difluoromethoxy, 3,5-difluorophenoxy, 3,4-difluorophenyl, 2,3-difluorophenoxy, 2,4-difluorophenoxy, 2,5-difluorophenoxy, 3,5-dimethoxyphenoxy,3-dimethylaminophenoxy, 3,4-dimethylbenzyloxy, 3,5-dimethylbenzyloxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 1,3-dioxolan-2-yl, 3-ethylbenzyloxy, 3-ethylphenoxy, 4-ethylaminophenoxy, 3-ethyl-5-methylphenoxy, 4-fluoro-3-methylbenzyl, 4-fluorobenzyloxy, 2-fluoro-3-methylphenoxy, 3-fluoro-4-methylphenoxy, 3-fluorophenoxy, 3-fluoro-2-nitrophenoxy, 2-fluoro-3-trifluoromethylbenzyloxy,

3-fluoro-5-trifluoromethylbenzyloxy, 2-fluorophenoxy, 4-fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2-fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4-trifluoromethylphenoxy, 2-furyl, 3-furyl, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, 2-hydroxy-3,3,3-trifluoropropoxy, isobutoxy, isobutyl, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, isopropoxy, 3-isopropylbenzyloxy, 3-isopropylphenoxy, isopropylthio, 4-isopropyl-3-methylphenoxy, 3-isothiazolyl, 4-isothiazolyl, 5-isothiazolyl, 3-methoxybenzyl, 4-methoxyphenylamino, 3-methylbenzyloxy, 4-methylbenxyloxy, 3-methylphenoxy, 3-methyl-4-methylthiophenoxy, 4-methylphenoxy, 1-methylpropoxy, 2-methylpyrid-5-yloxy, 4-methylthiophenoxy, 2-naphthyloxy, 2-nitrophenoxy, 4-nitrophenoxy, 3-nitrophenyl, 2-oxazolyl, 4-oxazolyl, 5-oxazolyl, pentafluoroethyl, pentafluoroethylthio, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, phenoxy, phenylamino, 1-phenylethoxy, 4-propylphenoxy, 4-propoxyphenoxy, thiophen-3-yl,tert -butoxy, 3-tert -butylphenoxy, 4-tert -butylphenoxy, 1,1,2,2-tetrafluoroethoxy, tetrahydrofuran-2-yl, 2-(5,6,7,8-tetrahydronaphthyloxy), thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, thiophen-2-yl, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, 3,3,3-trifluoro-2-hydroxypropyl, trifluoromethoxy, 3-trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, 4-trifluoromethoxyphenoxy, 3-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, 3-trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3-trifluoromethylphenyl, 2,3,4-trifluorophenoxy, 2,3,5-trifluorophenoxy, 3,4,5-trimethylphenoxy, 3-difluoromethoxyphenoxy, 3-pentafluoroethylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 3-trifluoromethylthiophenoxy, 3-trifluoromethylthiobenzyloxy, and trifluoromethylthio;

R_{11}, R_{31}, and R_{32} are independently selected from the group consisting of chloro, fluoro, hydrido, pentafluoroethyl, 1,1,2,2-tetrafluoroethoxy, and trifluoromethyl;

R_{30} is selected from the group consisting of chloro, ethyl, fluoro, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, isobutyl, isopropyl, methyl, pentafluoroethyl, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, propyl, *sec*-butyl, 1,1,2,2-tetrafluoroethoxy, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, trifluoromethoxy, and trifluoromethyl.

In an even more preferred specific embodiment of compounds of Formulas I-WOPC and I-WOHC,

A is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 4-methylcyclohexyl, 4-chloro-3-ethylphenoxycyclohexyl, 3-trifluoromethoxyphenoxycyclohexyl, 3-trifluoromethylcyclohexyl, 4-trifluoromethylcyclohexyl, 3,5-bis-trifluoromethylcyclohexyl, adamantyl, 3-trifluoromethyladamantyl, norbornyl, 3-trifluoromethylnorbornyl, norbornenyl, 7-oxabicyclo[2.2.1]heptan-2-yl, bicyclo[3.1.0]hexan-6-yl, 2-tetrahydrofuranyl, 3-tetrahydrofuranyl, 2-tetrahydropyranyl, 3-tetrahydropyranyl, 4-tetrahydropyranyl, 2-tetrahydrothienyl, and 3-tetrahydrothienyl, wherein a ring carbon other than the ring carbon at the point of attachment of A to Z may be optionally substituted with oxo provided that no more than one ring carbon is substituted by oxo at the same time, ring carbon and nitrogen atoms adjacent to the carbon atom at the point of attachment may be optionally substituted with R_9 or R_{13}, a ring carbon or nitrogen atom adjacent to the R_9 position and two atoms from the point of attachment may be substituted with R_{10}, a ring carbon or nitrogen atom adjacent to the R_{13} position and two atoms from the point of attachment may be substituted with R_{12}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{10} position may be substituted with R_{11}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{12} position may be substituted with R_{32}, and a

ring carbon or nitrogen atom four atoms from the point of attachment and adjacent to the R_{11} and R_{32} positions may be substituted with R_{31};

R_9 and R_{13} are fluoro;

R_{10} and R_{12} are independently selected from the group consisting of 5-bromo-2-fluorophenoxy, 4-chloro-3-ethylphenoxy, cyclopentyl, 2,3-dichlorophenoxy, 3,4-dichlorophenoxy, 3-difluoromethoxyphenoxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 3-ethylphenoxy, 3-ethyl-5-methylphenoxy, 4-fluoro-3-methylphenoxy, 4-fluorophenoxy, 2-furyl, isobutyl, isopropoxy, 3-isopropylphenoxy, 3-methylphenoxy, pentafluoroethyl, 3-pentafluoroethylphenoxy, 3-tert -butylphenoxy, 1,1,2,2-tetrafluoroethoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 2-(5,6,7,8-tetrahydronaphthyloxy),trifluoromethoxy, 3-trifluoromethoxybenzyloxy,3-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, trifluoromethylthio, and 3-trifluoromethylthiophenoxy;

R_{11}, R_{31}, and R_{32} are independently selected from the group consisting of chloro, fluoro, hydrido, pentafluoroethyl, 1,1,2,2-tetrafluoroethoxy, and trifluoromethyl.

DEFINITIONS

The use of generic terms in the description of the compounds are herein defined for clarity.

Standard single letter elemental symbols are used to represent specific types of atoms unless otherwise defined. The symbol "C" represents a carbon atom. The symbol "O" represents an oxygen atom. The symbol "N" represents a nitrogen atom. The symbol "P" represents a phosphorus atom. The symbol "S" represents a sulfur atom. The symbol "H" represents a hydrogen atom. Double letter elemental symbols are used as defined for the elements of the periodical table (i.e., Cl represents chlorine. Se represents selenium, etc.).

As utilized herein, the term "alkyl", either alone or within other terms such as "haloalkyl" and "alkylthio", means an acyclic alkyl radical containing from 1 to about 10, preferably from 3 to about 8 carbon atoms and more preferably 3 to

about 6 carbon atoms. Said alkyl radicals may be optionally substituted with groups as defined below. Examples of such radicals include methyl. ethyl, chloroethyl, hydroxyethyl, n-propyl, oxopropyl, isopropyl, n-butyl, cyanobutyl, isobutyl, sec-butyl, tert-butyl, pentyl, aminopentyl, iso-amyl, hexyl, octyl and the like.

The term "alkenyl" refers to an unsaturated, acyclic hydrocarbon radical in so much as it contains at least one double bond. Such alkenyl radicals contain from about 2 to about 10 carbon atoms, preferably from about 3 to about 8 carbon atoms and more preferably 3 to about 6 carbon atoms. Said alkenyl radicals may be optionally substituted with groups as defined below. Examples of suitable alkenyl radicals include propenyl, 2-chloropropenyl. buten-1-yl, isobutenyl, penten-1-yl, 2-2-methylbuten-1-yl, 3-methylbuten-1-yl, hexen-1-yl, 3-hydroxyhexen-1-yl, hepten-1-yl, and octen-1-yl. and the like.

The term "alkynyl" refers to an unsaturated, acyclic hydrocarbon radical in so much as it contains one or more triple bonds, such radicals containing about 2 to about 10 carbon atoms, preferably having from about 3 to about 8 carbon atoms and more preferably having 3 to about 6 carbon atoms. Said alkynyl radicals may be optionally substituted with groups as defined below. Examples of suitable alkynyl radicals include ethynyl, propynyl, hydroxypropynyl, butyn-1-yl, butyn-2-yl. pentyn-1-yl, pentyn-2-yl, 4-methoxypentyn-2-yl, 3-methylbutyn-1-yl, hexyn-1-yl, hexyn-2-yl, hexyn-3-yl, 3,3-dimethylbutyn-1-yl radicals and the like.

The term "hydrido" denotes a single hydrogen atom (H). This hydrido radical may be attached, for example, to an oxygen atom to form a "hydroxyl" radical, one hydrido radical may be attached to a carbon atom to form a "methine" radical (=CH-), or two hydrido radicals may be attached to a carbon atom to form a "methylene" (-CH_2-) radical.

The term "carbon" radical denotes a carbon atom without any covalent bonds and capable of forming four covalent bonds.

The term "cyano" radical denotes a carbon radical having three of four covalent bonds shared by a nitrogen atom.

The term "hydroxyalkyl" embraces radicals wherein any one or more of the alkyl carbon atoms is substituted with a hydroxyl as defined above. Specifically embraced are monohydroxyalkyl, dihydroxyalkyl and polyhydroxyalkyl radicals.

The term "alkanoyl" embraces radicals wherein one or more of the terminal alkyl carbon atoms are substituted with one or more carbonyl radicals as defined below. Specifically embraced are monocarbonylalkyl and dicarbonylalkyl radicals. Examples of monocarbonylalkyl radicals include formyl, acetyl, and pentanoyl. Examples of dicarbonylalkyl radicals include oxalyl, malonyl, and succinyl.

The term "alkylene" radical denotes linear or branched radicals having from 1 about 10 carbon atoms and having attachment points for two or more covalent bonds. Examples of such radicals are methylene, ethylene, ethylidene, methylethylene, and isopropylidene.

The term "alkenylene" radical denotes linear or branched radicals having from 2 to about 10 carbon atoms, at least one double bond, and having attachment points for two or more covalent bonds. Examples of such radicals are 1,1-vinylidene (CH_2=C), 1,2-vinylidene (-CH=CH-), and 1,4-butadienyl (-CH=CH-CH=CH-).

The term "halo" means halogens such as fluorine, chlorine, bromine or iodine atoms.

The term "haloalkyl" embraces radicals wherein any one or more of the alkyl carbon atoms is substituted with halo as defined above. Specifically embraced are monohaloalkyl, dihaloalkyl and polyhaloalkyl radicals. A monohaloalkyl radical, for one example, may have either a bromo, chloro or a fluoro atom within the radical. Dihalo radicals may have two or more of the same halo atoms or a combination of different halo radicals and polyhaloalkyl radicals may have more than two of the same halo atoms or a combination of different halo radicals. More preferred haloalkyl radicals are "lower haloalkyl" radicals having one to about six carbon atoms. Examples of such haloalkyl radicals include fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, trifluoroethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl and dichloropropyl.

The term "hydroxyhaloalkyl" embraces radicals wherein any one or more of the haloalkyl carbon atoms is substituted with hydroxy as defined above. Examples of "hydroxyhaloalkyl" radicals include hexafluorohydoxypropyl.

The term "haloalkylene radical" denotes alkylene radicals wherein any one or more of the alkylene carbon atoms is substituted with halo as defined above. Dihalo alkylene radicals may have two or more of the same halo atoms or a combination of different halo radicals and polyhaloalkylene radicals may have more than two of the same halo atoms or a combination of different halo radicals. More preferred haloalkylene radicals are "lower haloalkylene" radicals having one to about six carbon atoms. Examples of "haloalkylene" radicals include difluoromethylene, tetrafluoroethylene, tetrachloroethylene, alkyl substituted monofluoromethylene, and aryl substituted trifluoromethylene.

The term "haloalkenyl" denotes linear or branched radicals having from 1 to about 10 carbon atoms and having one or more double bonds wherein any one or more of the alkenyl carbon atoms is substituted with halo as defined above. Dihaloalkenyl radicals may have two or more of the same halo atoms or a combination of different halo radicals and polyhaloalkenyl radicals may have more than two of the same halo atoms or a combination of different halo radicals.

The terms "alkoxy" and "alkoxyalkyl" embrace linear or branched oxy-containing radicals each having alkyl portions of one to about ten carbon atoms, such as methoxy radical. The term "alkoxyalkyl" also embraces alkyl radicals having one or more alkoxy radicals attached to the alkyl radical, that is, to form monoalkoxyalkyl and dialkoxyalkyl radicals. More preferred alkoxy radicals are "lower alkoxy" radicals having one to six carbon atoms. Examples of such radicals include methoxy, ethoxy, propoxy, butoxy, isopropoxy and *tert*-butoxy alkyls. The "alkoxy" radicals may be further substituted with one or more halo atoms, such as fluoro, chloro or bromo, to provide "haloalkoxy" and "haloalkoxyalkyl" radicals. Examples of such haloalkoxy radicals include fluoromethoxy, chloromethoxy, trifluoromethoxy, difluoromethoxy, trifluoroethoxy, fluoroethoxy, tetrafluoroethoxy, pentafluoroethoxy, and fluoropropoxy. Examples of such haloalkoxyalkyl radicals include fluoromethoxymethyl, chloromethoxyethyl, trifluoromethoxymethyl, difluoromethoxyethyl, and trifluoroethoxymethyl.

The terms "alkenyloxy" and "alkenyloxyalkyl" embrace linear or branched oxy-containing radicals each having alkenyl portions of two to about ten carbon atoms, such as ethenyloxy or propenyloxy radical. The term "alkenyloxyalkyl" also embraces alkenyl radicals having one or more

alkenyloxy radicals attached to the alkyl radical, that is, to form monoalkenyloxyalkyl and dialkenyloxyalkyl radicals. More preferred alkenyloxy radicals are "lower alkenyloxy" radicals having two to six carbon atoms. Examples of such radicals include ethenyloxy, propenyloxy, butenyloxy, and isopropenyloxy alkyls. The "alkenyloxy" radicals may be further substituted with one or more halo atoms, such as fluoro, chloro or bromo, to provide "haloalkenyloxy" radicals. Examples of such radicals include trifluoroethenyloxy, fluoroethenyloxy, difluoroethenyhloxy, and fluoropropenyloxy.

The term "haloalkoxyalkyl" also embraces alkyl radicals having one or more haloalkoxy radicals attached to the alkyl radical, that is, to form monohaloalkoxyalkyl and dihaloalkoxyalkyl radicals. The term "haloalkenyloxy" also embraces oxygen radicals having one or more haloalkenyloxy radicals attached to the oxygen radical, that is, to form monohaloalkenyloxy and dihaloalkenyloxy radicals. The term "haloalkenyloxyalkyl" also embraces alkyl radicals having one or more haloalkenyloxy radicals attached to the alkyl radical, that is, to form monohaloalkenyloxyalkyl and dihaloalkenyloxyalkyl radicals.

The term "alkylenedioxy" radicals denotes alkylene radicals having at least two oxygens bonded to a single alkylene group. Examples of "alkylenedioxy" radicals include methylenedioxy, ethylenedioxy, alkylsubstituted methylenedioxy, and arylsubstituted methylenedioxy. The term "haloalkylenedioxy" radicals denotes haloalkylene radicals having at least two oxy groups bonded to a single haloalkyl group. Examples of "haloalkylenedioxy" radicals include difluoromethylenedioxy, tetrafluoroethylenedioxy, tetrachloroethylenedioxy, alkylsubstituted monofluoromethylenedioxy, and arylsubstituted monofluoromethylenedioxy.

The term "aryl", alone or in combination, means a carbocyclic aromatic system containing one, two or three rings wherein such rings may be attached together in a pendant manner or may be fused. The term "fused" means that a second ring is present (ie, attached or formed) by having two adjacent atoms in common (ie, shared) with the first ring. The term "fused" is equivalent to the term "condensed". The term "aryl" embraces aromatic radicals such as phenyl, naphthyl, tetrahydronaphthyl, indane and biphenyl.

The term "perhaloaryl" embraces aromatic radicals such as phenyl, naphthyl, tetrahydronaphthyl, indane and biphenyl wherein the aryl radical is substituted with 3 or more halo radicals as defined below.

The term "heterocyclyl" embraces saturated and partially saturated heteroatom-containing ring-shaped radicals having from 5 through 15 ring members selected from carbon, nitrogen, sulfur and oxygen, wherein at least one ring atom is a heteroatom. Heterocyclyl radicals may contain one, two or three rings wherein such rings may be attached in a pendant manner or may be fused. Examples of saturated heterocyclic radicals include saturated 3 to 6-membered heteromonocylic group containing 1 to 4 nitrogen atoms[e.g. pyrrolidinyl, imidazolidinyl, piperidino, piperazinyl, etc.]; saturated 3 to 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms [e.g. morpholinyl, etc.]; saturated 3 to 6-membered heteromonocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms [e.g., thiazolidinyl, etc.]. Examples of partially saturated heterocyclyl radicals include dihydrothiophene, dihydropyran, dihydrofuran and dihydrothiazole. Non-limiting examples of heterocyclic radicals include 2-pyrrolinyl, 3-pyrrolinyl, pyrrolindinyl, 1,3-dioxolanyl, 2H-pyranyl, 4H-pyranyl, piperidinyl, 1,4-dioxanyl, morpholinyl, 1,4-dithianyl, thiomorpholinyl, and the like.

The term "heteroaryl" embraces fully unsaturated heteroatom-containing ring-shaped aromatic radicals having from 5 through 15 ring members selected from carbon, nitrogen, sulfur and oxygen, wherein at least one ring atom is a heteroatom. Heteroaryl radicals may contain one, two or three rings wherein such rings may be attached in a pendant manner or may be fused. Examples of "heteroaryl" radicals, include unsaturated 5 to 6 membered heteromonocyclyl group containing 1 to 4 nitrogen atoms, for example, pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl [e.g., 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl, etc.] tetrazolyl [e.g. 1H-tetrazolyl, 2H-tetrazolyl, etc.], etc.; unsaturated condensed heterocyclic group containing 1 to 5 nitrogen atoms, for example, indolyl, isoindolyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl, tetrazolopyridazinyl [e.g., tetrazolo [1,5-b]pyridazinyl, etc.], etc.; unsaturated 3 to 6-membered heteromonocyclic group containing an oxygen atom, for example, pyranyl, 2-furyl, 3-furyl, etc.; unsaturated 5 to 6-membered heteromonocyclic group containing a sulfur atom,

for example, 2-thienyl, 3-thienyl, etc.: unsaturated 5- to 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, for example, oxazolyl, isoxazolyl, oxadiazolyl [e.g., 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl, etc.] etc.; unsaturated condensed heterocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms [e.g. benzoxazolyl, benzoxadiazolyl, etc.]; unsaturated 5 to 6-membered heteromonocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms, for example, thiazolyl, thiadiazolyl [e.g., 1,2,4- thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl, etc.] etc.; unsaturated condensed heterocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms [e.g., benzothiazolyl, benzothiadiazolyl, etc.] and the like. The term also embraces radicals where heterocyclic radicals are fused with aryl radicals. Examples of such fused bicyclic radicals include benzofuran, benzothiophene, and the like. Said "heterocyclyl" group may have 1 to 3 substituents as defined below. Preferred heterocyclic radicals include five to twelve membered fused or unfused radicals. Non-limiting examples of heteroaryl radicals include pyrrolyl, pyridinyl, pyridyloxy, pyrazolyl, triazolyl, pyrimidinyl, pyridazinyl, oxazolyl, thiazolyl, imidazolyl, indolyl, thiophenyl, furanyl, tetrazolyl, 2-imidazolinyl, imidazolidinyl, 2-pyrazolinyl, pyrazolidinyl, isoxazolyl, isothiazolyl, 1,2,3-oxadiazolyl, 1,2,3-triazolyl, 1,3,4-thiadiazolyl, pyrazinyl, piperazinyl, 1,3,5-triazinyl, 1,3,5-trithianyl, benzo(b)thiophenyl, benzimidazoyl, quinolinyl, tetraazolyl, and the like.

The term "sulfonyl", whether used alone or linked to other terms such as alkylsulfonyl, denotes respectively divalent radicals $-SO_2-$. "Alkylsulfonyl", embraces alkyl radicals attached to a sulfonyl radical, where alkyl is defined as above. "Alkylsulfonylalkyl", embraces alkylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above. "Haloalkylsulfonyl", embraces haloalkyl radicals attached to a sulfonyl radical, where haloalkyl is defined as above. "Haloalkylsulfonylalkyl", embraces haloalkylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above. The term "aminosulfonyl" denotes an amino radical attached to a sulfonyl radical.

The term "sulfinyl", whether used alone or linked to other terms such as alkylsulfinyl, denotes respectively divalent radicals -S(O)-. "Alkylsulfinyl", embraces alkyl radicals attached to a sulfinyl radical, where alkyl is defined as above. "Alkylsulfinylalkyl", embraces alkylsulfinyl radicals attached to an alkyl

radical, where alkyl is defined as above. "Haloalkylsulfinyl", embraces haloalkyl radicals attached to a sulfinyl radical, where haloalkyl is defined as above. "Haloalkylsulfinylalkyl", embraces haloalkylsulfinyl radicals attached to an alkyl radical, where alkyl is defined as above.

The term "aralkyl" embraces aryl-substituted alkyl radicals. Preferable aralkyl radicals are "lower aralkyl" radicals having aryl radicals attached to alkyl radicals having one to six carbon atoms. Examples of such radicals include benzyl, diphenylmethyl, triphenylmethyl, phenylethyl and diphenylethyl. The terms benzyl and phenylmethyl are interchangeable.

The term "heteroaralkyl" embraces heteroaryl-substituted alkyl radicals wherein the heteroaralkyl radical may be additionally substituted with three or more substituents as defined above for aralkyl radicals. The term "perhaloaralkyl" embraces aryl-substituted alkyl radicals wherein the aralkyl radical is substituted with three or more halo radicals as defined above.

The term "aralkylsulfinyl", embraces aralkyl radicals attached to a sulfinyl radical, where aralkyl is defined as above. "Aralkylsulfinylalkyl", embraces aralkylsulfinyl radicals attached to an alkyl radical, where alkyl is defined as above.

The term "aralkylsulfonyl", embraces aralkyl radicals attached to a sulfonyl radical, where aralkyl is defined as above. "Aralkylsulfonylalkyl", embraces aralkylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above.

The term "cycloalkyl" embraces radicals having from 3 through 15 carbon atoms. Cycloalkyl radicals may contain one, two, three, or four rings wherein such rings may be attached in a pendant manner or may be fused. Examples of cycloalkyl radicals having two or more rings include adamantyl, norbornyl, and 7-oxabicyclo[2.2.1]heptanyl. More preferred cycloalkyl radicals are "lower cycloalkyl" radicals having from 3 through 8 carbon atoms. Examples include radicals such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl. The term "cycloalkyl" also embraces radicals where cycloalkyl radicals are fused with aryl radicals or heterocyclyl radicals. The term "cycloalkylalkyl" embraces cycloalkyl-substituted alkyl radicals. Preferable cycloalkylalkyl radicals are "lower cycloalkylalkyl" radicals having cycloalkyl radicals attached to alkyl radicals having from one through six carbon atoms. Examples of such radicals include cyclohexylhexyl. The term "cycloalkenyl" embraces radicals having three to fifteen carbon atoms and one

or more carbon-carbon double bonds. Cycloalkenyl radicals may contain one, two, three, or four rings wherein such rings may be attached in a pendant manner or may be fused. Examples of cycloalkenyl radicals having two or more rings include norbornenyl. Preferred cycloalkenyl radicals are "lower cycloalkenyl" radicals having three to seven carbon atoms. Examples include radicals such as cyclobutenyl, cyclopentenyl, cyclohexenyl and cycloheptenyl. The term "halocycloalkyl" embraces radicals wherein any one or more of the cycloalkyl carbon atoms is substituted with halo as defined above. Specifically embraced are monohalocycloalkyl, dihalocycloalkyl and polyhalocycloalkyl radicals. A monohalocycloalkyl radical, for one example, may have either a bromo, chloro or a fluoro atom within the radical. Dihalo radicals may have two or more of the same halo atoms or a combination of different halo radicals and polyhalocycloalkyl radicals may have more than two of the same halo atoms or a combination of different halo radicals. More preferred halocycloalkyl radicals are "lower halocycloalkyl" radicals having three to about eight carbon atoms. Examples of such halocycloalkyl radicals include fluorocyclopropyl, difluorocyclobutyl, trifluorocyclopentyl, tetrafluorocyclohexyl, and dichlorocyclopropyl. The term "halocycloalkenyl" embraces radicals wherein any one or more of the cycloalkenyl carbon atoms is substituted with halo as defined above. Specifically embraced are monohalocycloalkenyl, dihalocycloalkenyl and polyhalocycloalkenyl radicals.

The term "cycloalkoxy" embraces cycloalkyl radicals attached to an oxy radical. Examples of such radicals includes cyclohexoxy and cyclopentoxy. The term "cycloalkoxyalkyl" also embraces alkyl radicals having one or more cycloalkoxy radicals attached to the alkyl radical, that is, to form monocycloalkoxyalkyl and dicycloalkoxyalkyl radicals. Examples of such radicals include cyclohexoxyethyl. The "cycloalkoxy" radicals may be further substituted with one or more halo atoms, such as fluoro, chloro or bromo, to provide "halocycloalkoxy" and "halocycloalkoxyalkyl" radicals.

The term "cycloalkylalkoxy" embraces cycloalkyl radicals attached to an alkoxy radical. Examples of such radicals includes cyclohexylmethoxy and cyclopentylmethoxy.

The term "cycloalkenyloxy" embraces cycloalkenyl radicals attached to an oxy radical. Examples of such radicals includes cyclohexenyloxy and cyclopentenyloxy. The term "cycloalkenyloxyalkyl" also embraces alkyl radicals having one or more cycloalkenyloxy radicals attached to the alkyl

radical, that is, to form monocycloalkenyloxyalkyl and dicycloalkenyloxyalkyl radicals. Examples of such radicals include cyclohexenyloxyethyl. The "cycloalkenyloxy" radicals may be further substituted with one or more halo atoms, such as fluoro, chloro or bromo, to provide "halocycloalkenyloxy" and "halocycloalkenyloxyalkyl" radicals.

The term "cycloalkylenedioxy" radicals denotes cycloalkylene radicals having at least two oxygens bonded to a single cycloalkylene group. Examples of "alkylenedioxy" radicals include 1,2-dioxycyclohexylene.

The term "cycloalkylsulfinyl", embraces cycloalkyl radicals attached to a sulfinyl radical, where cycloalkyl is defined as above. "Cycloalkylsulfinylalkyl", embraces cycloalkylsulfinyl radicals attached to an alkyl radical, where alkyl is defined as above. The term "Cycloalkylsulfonyl", embraces cycloalkyl radicals attached to a sulfonyl radical, where cycloalkyl is defined as above. "Cycloalkylsulfonylalkyl", embraces cycloalkylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above.

The term "cycloalkylalkanoyl" embraces radicals wherein one or more of the cycloalkyl carbon atoms are substituted with one or more carbonyl radicals as defined below. Specifically embraced are monocarbonylcycloalkyl and dicarbonylcycloalkyl radicals. Examples of monocarbonylcycloalkyl radicals include cyclohexylcarbonyl, cyclohexylacetyl, and cyclopentylcarbonyl. Examples of dicarbonylcycloalkyl radicals include 1,2-dicarbonylcyclohexane..

The term "alkylthio" embraces radicals containing a linear or branched alkyl radical, of one to ten carbon atoms, attached to a divalent sulfur atom. More preferred alkylthio radicals are "lower alkylthio" radicals having one to six carbon atoms. An example of "lower alkylthio" is methylthio (CH_3-S-). The "alkylthio" radicals may be further substituted with one or more halo atoms, such as fluoro, chloro or bromo, to provide "haloalkylthio" radicals. Examples of such radicals include fluoromethylthio, chloromethylthio, trifluoromethylthio, difluoromethylthio, trifluoroethylthio, fluoroethylthio, tetrafluoroethylthio, pentafluoroethylthio, and fluoropropylthio.

The term "alkyl aryl amino" embraces radicals containing a linear or branched alkyl radical, of one to ten carbon atoms, and one aryl radical both attached to an amino radical. Examples include N-methyl-4-methoxyaniline, N-ethyl-4-methoxyaniline, and N-methyl-4-trifluoromethoxyaniline.

The terms alkylamino denotes "monoalkylamino" and "dialkylamino" containing one or two alkyl radicals, respectively, attached to an amino radical.

The terms arylamino denotes "monoarylamino" and "diarylamino" containing one or two aryl radicals, respectively, attached to an amino radical. Examples of such radicals include N-phenylamino and N-naphthylamino.

The term "aralkylamino", embraces aralkyl radicals attached to an amino radical, where aralkyl is defined as above. The term aralkylamino denotes "monoaralkylamino" and "diaralkylamino" containing one or two aralkyl radicals, respectively, attached to an amino radical. The term aralkylamino further denotes "monoaralkyl monoalkylamino" containing one aralkyl radical and one alkyl radical attached to an amino radical.

The term "arylsulfinyl" embraces radicals containing an aryl radical, as defined above, attached to a divalent S(=O) atom. The term "arylsulfinylalkyl" denotes arylsulfinyl radicals attached to a linear or branched alkyl radical, of one to ten carbon atoms.

The term "arylsulfonyl", embraces aryl radicals attached to a sulfonyl radical, where aryl is defined as above. "arylsulfonylalkyl", embraces arylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above. The term "heteroarylsulfinyl" embraces radicals containing an heteroaryl radical, as defined above, attached to a divalent S(=O) atom. The term "heteroarylsulfinylalkyl" denotes heteroarylsulfinyl radicals attached to a linear or branched alkyl radical, of one to ten carbon atoms. The term "Heteroarylsulfonyl", embraces heteroaryl radicals attached to a sulfonyl radical, where heteroaryl is defined as above. "Heteroarylsulfonylalkyl", embraces heteroarylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above.

The term "aryloxy" embraces aryl radicals, as defined above, attached to an oxygen atom. Examples of such radicals include phenoxy, 4-chloro-3-ethylphenoxy, 4-chloro-3-methylphenoxy, 3-chloro-4-ethylphenoxy, 3,4-dichlorophenoxy, 4-methylphenoxy, 3-trifluoromethoxyphenoxy, 3-trifluoromethylphenoxy, 4-fluorophenoxy, 3,4-dimethylphenoxy, 5-bromo-2-fluorophenoxy, 4-bromo-3-fluorophenoxy, 4-fluoro-3-methylphenoxy, 5,6,7,8-tetrahydronaphthyloxy, 3-isopropylphenoxy, 3-cyclopropylphenoxy, 3-ethylphenoxy, 4-*tert* -butylphenoxy, 3-pentafluoroethylphenoxy, and 3-(1,1,2,2-tetrafluoroethoxy)phenoxy.

The term "aroyl" embraces aryl radicals, as defined above, attached to an carbonyl radical as defined above. Examples of such radicals include benzoyl and toluoyl.

The term "aralkanoyl" embraces aralkyl radicals, as defined herein, attached to an carbonyl radical as defined above. Examples of such radicals include, for example, phenylacetyl.

The term "aralkoxy" embraces oxy-containing aralkyl radicals attached through an oxygen atom to other radicals. More preferred aralkoxy radicals are "lower aralkoxy" radicals having phenyl radicals attached to lower alkoxy radical as described above. Examples of such radicals include benzyloxy, 1-phenylethoxy, 3-trifluoromethoxybenzyloxy, 3-trifluoromethylbenzyloxy, 3,5-difluorobenyloxy, 3-bromobenzyloxy, 4-propylbenzyloxy, 2-fluoro-3-trifluoromethylbenzyloxy, and 2-phenylethoxy.

The term "aryloxyalkyl" embraces aryloxy radicals, as defined above, attached to an alkyl group. Examples of such radicals include phenoxymethyl.

The term "haloaryloxyalkyl" embraces aryloxyalkyl radicals, as defined above, wherein one to five halo radicals are attached to an aryloxy group.

The term "heteroaroyl" embraces heteroaryl radicals, as defined above, attached to an carbonyl radical as defined above. Examples of such radicals include furoyl and nicotinyl.

The term "heteroaralkanoyl" embraces heteroaralkyl radicals, as defined herein, attached to an carbonyl radical as defined above. Examples of such radicals include, for example, pyridylacetyl and furylbutyryl.

The term "heteroaralkoxy" embraces oxy-containing heteroaralkyl radicals attached through an oxygen atom to other radicals. More preferred heteroaralkoxy radicals are "lower heteroaralkoxy" radicals having heteroaryl radicals attached to lower alkoxy radical as described above.

The term "haloheteroaryloxyalkyl" embraces heteroaryloxyalkyl radicals, as defined above, wherein one to four halo radicals are attached to an heteroaryloxy group.

The term "heteroarylamino" embraces heterocyclyl radicals, as defined above, attached to an amino group. Examples of such radicals include pyridylamino.

The term "heteroarylaminoalkyl" embraces heteroarylamino radicals, as defined above, attached to an alkyl group. Examples of such radicals include pyridylmethylamino.

The term "heteroaryloxy" embraces heterocyclyl radicals, as defined above, attached to an oxy group. Examples of such radicals include 2-thiophenyloxy, 2-pyrimidyloxy, 2-pyridyloxy, 3-pyridyloxy, and 4-pyridyloxy.

The term "heteroaryloxyalkyl" embraces heteroaryloxy radicals, as defined above, attached to an alkyl group. Examples of such radicals include 2-pyridyloxymethyl, 3-pyridyloxyethyl, and 4-pyridyloxymethyl.

The term "arylthio" embraces aryl radicals, as defined above, attached to an sulfur atom. Examples of such radicals include phenylthio.

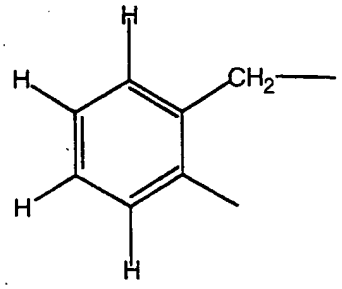
The term "arylthioalkyl" embraces arylthio radicals, as defined above, attached to an alkyl group. Examples of such radicals include phenylthiomethyl.

The term "alkylthioalkyl" embraces alkylthio radicals, as defined above, attached to an alkyl group. Examples of such radicals include methylthiomethyl. The term "alkoxyalkyl" embraces alkoxy radicals, as defined above, attached to an alkyl group. Examples of such radicals include methoxymethyl.

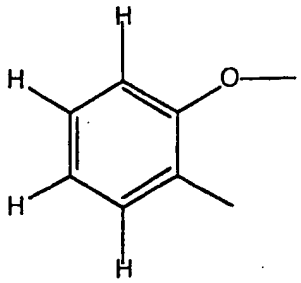
The term "carbonyl" denotes a carbon radical having two of the four covalent bonds shared with an oxygen atom. The term "carboxy" embraces a hydroxyl radical, as defined above, attached to one of two unshared bonds in a carbonyl group. The term "carboxamide" embraces amino, monoalkylamino, dialkylamino, monocycloalkylamino, alkylcycloalkylamino, and dicycloalkylamino radicals, attached to one of two unshared bonds in a carbonyl group. The term "carboxamidoalkyl" embraces carboxamide radicals, as defined above, attached to an alkyl group. The term "carboxyalkyl" embraces a carboxy radical, as defined above, attached to an alkyl group. The term "carboalkoxy" embraces alkoxy radicals, as defined above, attached to one of two unshared bonds in a carbonyl group. The term "carboaralkoxy" embraces aralkoxy radicals, as defined above, attached to one of two unshared bonds in a carbonyl group. The term "monocarboalkoxyalkyl" embraces one carboalkoxy radical, as defined above, attached to an alkyl group. The term "dicarboalkoxyalkyl" embraces two carboalkoxy radicals, as defined above, attached to an alkylene group. The term "monocyanoalkyl" embraces one cyano radical, as defined above, attached to an alkyl group. The term "dicyanoalkylene" embraces two cyano radicals, as defined above, attached to an alkyl group. The term "carboalkoxycyanoalkyl" embraces one cyano radical, as defined above, attached to an carboalkoxyalkyl group.

The term "acyl", alone or in combination, means a carbonyl or thionocarbonyl group bonded to a radical selected from, for example, hydrido, alkyl, alkenyl, alkynyl, haloalkyl, alkoxy, alkoxyalkyl, haloalkoxy, aryl, heterocyclyl, heteroaryl, alkylsulfinylalkyl, alkylsulfonylalkyl, aralkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, alkylthio, arylthio, amino, alkylamino, dialkylamino, aralkoxy, arylthio, and alkylthioalkyl. Examples of "acyl" are formyl, acetyl, benzoyl, trifluoroacetyl, phthaloyl, malonyl, nicotinyl, and the like. The term "haloalkanoyl" embraces one or more halo radicals, as defined herein, attached to an alkanoyl radical as defined above. Examples of such radicals include, for example, chloroacetyl, trifluoroacetyl, bromopropanoyl, and heptafluorobutanoyl. The term "diacyl", alone or in combination, means having two or more carbonyl or thionocarbonyl groups bonded to a radical selected from, for example, alkylene, alkenylene, alkynylene, haloalkylene, alkoxyalkylene, aryl, heterocyclyl, heteroaryl, aralkyl, cycloalkyl, cycloalkylalkyl, and cycloalkenyl. Examples of "diacyl" are phthaloyl, malonyl, succinyl, adipoyl, and the like.

The term "benzylidenyl" radical denotes substituted and unsubstituted benzyl groups having attachment points for two covalent bonds. One attachment point is through the methylene of the benzyl group with the other attachment point through an ortho carbon of the phenyl ring. The methylene group is designated for attached to the lowest numbered position. Examples include the base compound benzylidene of structure:



The term "phenoxylidenyl" radical denotes substituted and unsubstituted phenoxy groups having attachment points for two covalent bonds. One attachment point is through the oxy of the phenoxy group with the other attachment point through an ortho carbon of the phenyl ring. The oxy group is designated for attached to the lowest numbered position. Examples include the base compound phenoxylidene of structure:



The term "phosphono" embraces a pentavalent phosphorus attached with two covalent bonds to an oxygen radical. The term "dialkoxyphosphono" denotes two alkoxy radicals, as defined above, attached to a phosphono radical with two covalent bonds. The term "diaralkoxyphosphono" denotes two aralkoxy radicals, as defined above, attached to a phosphono radical with two covalent bonds. The term "dialkoxyphosphonoalkyl" denotes dialkoxyphosphono radicals, as defined above, attached to an alkyl radical. The term "diaralkoxyphosphonoalkyl" denotes diaralkoxyphosphono radicals, as defined above, attached to an alkyl radical.

Said "alkyl", "alkenyl", "alkynyl", "alkanoyl", "alkylene", "alkenylene", "benzylidenyl", "phenoxylidenyl", "hydroxyalkyl", "haloalkyl", "haloalkylene", "haloalkenyl", "alkoxy", "alkenyloxy", "alkenyloxyalkyl", "alkoxyalkyl", "aryl", "perhaloaryl", "haloalkoxy", "haloalkoxyalkyl", "haloalkenyloxy", "haloalkenyloxyalkyl", "alkylenedioxy", "haloalkylenedioxy", "heterocyclyl", "heteroaryl", "hydroxyhaloalkyl", "alkylsulfonyl", "haloalkylsulfonyl", "alkylsulfonylalkyl", "haloalkylsulfonylalkyl", "alkylsulfinyl", "alkylsulfinylalkyl", "haloalkylsulfinylalkyl", "aralkyl", "heteroaralkyl", "perhaloaralkyl", "aralkylsulfonyl", "aralkylsulfonylalkyl", "aralkylsulfinyl", "aralkylsulfinylalkyl", "cycloalkyl", "cycloalkylalkanoyl", "cycloalkylalkyl", "cycloalkenyl", "halocycloalkyl", "halocycloalkenyl", "cycloalkylsulfinyl", "cycloalkylsulfinylalkyl", "cycloalkylsulfonyl", "cycloalkylsulfonylalkyl", "cycloalkoxy", "cycloalkoxyalkyl", "cycloalkylalkoxy", "cycloalkenyloxy", "cycloalkenyloxyalkyl", "cycloalkylenedioxy", "halocycloalkoxy", "halocycloalkoxyalkyl", "halocycloalkenyloxy", "halocycloalkenyloxyalkyl", "alkylthio", "haloalkylthio", "alkylsulfinyl", "amino", "oxy", "thio", "alkylamino", "arylamino", "aralkylamino", "arylsulfinyl", "arylsulfinylalkyl", "arylsulfonyl", "arylsulfonylalkyl", "heteroarylsulfinyl", "heteroarylsulfinylalkyl", "heteroarylsulfonyl", "heteroarylsulfonylalkyl", "heteroarylamino", "heteroarylaminoalkyl", "heteroaryloxy", "heteroaryloxylalkyl", "aryloxy",

"aroyl", "aralkanoyl", "aralkoxy", "aryloxyalkyl", "haloaryloxyalkyl", "heteroaroyl", "heteroaralkanoyl", "heteroaralkoxy", "heteroaralkoxyalkyl", "arylthio", "arylthioalkyl", "alkoxyalkyl", "acyl" and "diacyl" groups defined above may optionally have 1 to 5 non-hydrido substituents such as perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, aralkylsulfinyl, aralkylsulfinylalkyl, halocycloalkyl, halocycloalkenyl, cycloalkylsulfinyl, cycloalkylsulfinylalkyl, cycloalkylsulfonyl, cycloalkylsulfonylalkyl, heteroarylamino, N-heteroarylamino-N-alkylamino, heteroarylaminoalkyl, heteroaryloxy, heteroaryloxylalkyl, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, haloalkoxylalkyl, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, cycloalkoxyalkyl, cycloalkylalkoxy, cycloalkenyloxyalkyl, cycloalkylenedioxy, halocycloalkoxy, halocycloalkoxyalkyl, halocycloalkenyloxy, halocycloalkenyloxyalkyl, hydroxy, amino, thio, nitro, lower alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylthioalkyl, heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, arylsulfonylalkyl, heteroarylsulfinylalkyl, heteroarylsulfonylalkyl, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfinylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, monoarylamidosulfonyl, arylsulfonamido, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, alkenyloxy, alkenyloxyalky, alkylenedioxy, haloalkylenedioxy, cycloalkyl, cycloalkylalkanoyl, cycloalkenyl, lower cycloalkylalkyl, lower cycloalkenylalkyl, halo, haloalkyl, haloalkenyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydoxyheteroaralkyl, haloalkoxyalkyl, aryl, aralkyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, heteroarylalkenyl, carboxyalkyl, carboalkoxy, alkoxycarbonyl, carboaralkoxy, carboxamido, carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl.

The term "spacer" may include a covalent bond, a linear moiety having a backbone of 1 to 7 continous atoms, and a branched moiety having three branches connecting to a common atom with a total of from 1 through 8 atoms. The spacer may have 1 to 7 atoms of a univalent or multi-valent chain. Univalent chains may be constituted by a radical selected from =C(H)-,

$=C(R_{17})$-, -O-, -S-, -S(O)-, $-S(O)_2$-, -NH-, $-N(R_{17})$-, -N=, -CH(OH)-, $=C(OH)$-, $-CH(OR_{17})$-, $=C(OR_{17})$-, and -C(O)- wherein R_{17} is selected from alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, aryloxyalkyl, alkoxyalkyl, alkylthioalkyl, arylthioalkyl, cycloalkyl, cycloalkylalkyl, haloalkyl, haloalkenyl, haloalkoxyalkyl, perhaloaralkyl, heteroarylalkyl, heteroaryloxyalkyl, heteroarylthioalkyl, and heteroarylalkenyl. Multi-valent chains may consist of a straight chain of 1 or 2 or 3 or 4 or 5 or 6 or 7 atoms, a straight chain of 1 or 2 or 3 or 4 or 5 or 6 atoms with a side chain, or a branched chain made up of 1 or 2 or 3 or 4 atoms in each of the three branches. The chain may be constituted of one or more radicals selected from: lower alkylene, lower alkenyl, -O-, $-O-CH_2$-, $-S-CH_2$-, $-CH_2CH_2$-, ethenyl, -CH=CH(OH)-, $-OCH_2O$-, $-O(CH_2)_2O$-, $-NHCH_2$-, $-OCH(R_{17})O$-, $-O(CH_2CHR_{17})O$-, $-OCF_2O$-, $-O(CF_2)_2O$-, -S-, -S(O)-, $-S(O)_2$-, -N(H)-, -N(H)O-, $-N(R_{17})O$-, $-N(R_{17})$-, -C(O)-, -C(O)NH-, $-C(O)NR_{17}$-, -N=, $-OCH_2$-, $-SCH_2$-, $S(O)CH_2$-, $-CH_2C(O)$-, -CH(OH)-, $=C(OH)$-, $-CH(OR_{17})$-, $=C(OR_{17})$-, $S(O)_2CH_2$-, and $-NR_{17}CH_2$- and many other radicals defined above or generally known or ascertained by one of skill-in-the art. Side chains may include substituents such as 1 to 5 non-hydrido substituents such as perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, aralkylsulfinyl, aralkylsulfinylalkyl, halocycloalkyl, halocycloalkenyl, cycloalkylsulfinyl, cycloalkylsulfinylalkyl, cycloalkylsulfonyl, cycloalkylsulfonylalkyl, heteroarylamino, N-heteroarylamino-N-alkylamino, heteroarylaminoalkyl, heteroaryloxy, heteroaryloxylalkyl, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, haloalkoxylalkyl, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, cycloalkoxyalkyl, cycloalkylalkoxy, cycloalkenyloxyalkyl, cycloalkylenedioxy, halocycloalkoxy, halocycloalkoxyalkyl, halocycloalkenyloxy, halocycloalkenyloxyalkyl, hydroxy, amino, thio, nitro, lower alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylthioalkyl, heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, arylsulfonylalkyl,

heteroarylsulfinylalkyl, heteroarylsulfonylalkyl, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfinylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, monoarylamidosulfonyl, arylsulfonamido, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, alkenyloxy, alkenyloxyalky, alkylenedioxy, haloalkylenedioxy, cycloalkyl, cycloalkenyl, lower cycloalkylalkyl, lower cycloalkenylalkyl, halo, haloalkyl, haloalkenyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydoxyheteroaralkyl, haloalkoxyalkyl, aryl, aralkyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, heteroarylalkenyl, carboxyalkyl, carboalkoxy, carboaralkoxy, carboxamido, carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl.

Compounds of the present invention can exist in tautomeric, geometric or stereoisomeric forms. The present invention contemplates all such compounds, including cis- and trans-geometric isomers, E- and Z-geometric isomers, R- and S-enantiomers, diastereomers, d-isomers, l-isomers, the racemic mixtures thereof and other mixtures thereof, as falling within the scope of the invention. Pharmaceutically acceptable sales of such tautomeric, geometric or stereoisomeric forms are also included within the invention.

The terms "cis" and "trans" denote a form of geometric isomerism in which two carbon atoms connected by a double bond will each have a hydrogen atom on the same side of the double bond ("cis") or on opposite sides of the double bond ("trans").

Some of the compounds described contain alkenyl groups, and are meant to include both cis and trans or "E" and "Z" geometric forms.

Some of the compounds described contain one or more stereocenters and are meant to include R, S, and mixtures of R and S forms for each stereocenter present.

Some of the compounds described herein may contain one or more ketonic or aldehydic carbonyl groups or combinations thereof alone or as part of a heterocyclic ring system. Such carbonyl groups may exist in part or

principally in the "keto" form and in part or principally as one or more "enol" forms of each aldehyde and ketone group present. Compounds of the present invention having aldehydic or ketonic carbonyl groups are meant to include both "keto" and "enol" tautomeric forms.

Some of the compounds described herein may contain one or more amide carbonyl groups or combinations thereof alone or as part of a heterocyclic ring system. Such carbonyl groups may exist in part or principally in the "keto" form and in part or principally as one or more "enol" forms of each amide group present. Compounds of the present invention having amidic carbonyl groups are meant to include both "keto" and "enol" tautomeric forms. Said amide carbonyl groups may be both oxo (C=O) and thiono (C=S) in type.

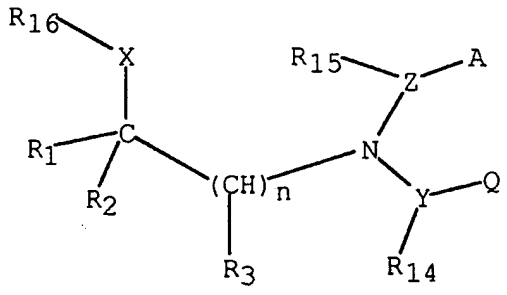
Some of the compounds described herein may contain one or more imine or enamine groups or combinations thereof. Such groups may exist in part or principally in the "imine" form and in part or principally as one or more "enamine" forms of each group present. Compounds of the present invention having said imine or enamine groups are meant to include both "imine" and "enamine" tautomeric forms.

The following general synthetic sequences are useful in making the present invention. Abbreviations used in the schemes are as follows: "AA" represents amino acids, "BINAP" represents 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl, "Boc" represents tert-butyloxycarbonyl, "BOP" represents benzotriazol-1-yl-oxy-tris-(dimethylamino), "bu" represents butyl, "dba" represents dibenzylideneacetone, "DCC" represents 1,3-dicyclohexylcarbodiimide, "DIBAH" represents diisobutylaluminum hydride, "DIPEA" represents diisopropylethylamine, "DMF" represents dimethylformamide, "DMSO" represents dimethylsulfoxide, "Fmoc" represents 9-fluorenylmethoxycarbonyl, "LDA" represents lithium diisopropylamide, "PHTH" represents a phthaloyl group, "pnZ" represents 4-nitrobenzyloxycarbonyl, "PTC" represents a phase transfer catalyst, "p-TsOH" represents paratoluenesulfonic acid, "TBAF" represents tetrabutylammonium fluoride, "TBTU" represents 2-(1H-benzotriozole-1-yl)-1,1,3,3-tetramethyl uronium tetrafluoroborate, "TEA" represents triethylamine, "TFA" represents trifluoroacetic acid, "THF" represents tetrahydrofuran, "TMS" represents trimethylsilyl, and "Z" represents benzyloxycarbonyl.

PHARMACEUTICAL UTILITY AND COMPOSITION

The present invention comprises a pharmaceutical composition comprising a therapeutically-effective amount of a compound of Formulas VII-H, VII, VII-2, VII-3, VII-4, and Cyclo-VII, in association with at least one pharmaceutically-acceptable carrier, adjuvant or diluent.

The present invention also comprises a treatment and prophylaxis of coronary artery disease and other CETP-mediated disorders in a subject, comprising administering to the subject having such disorder a therapeutically-effective amount of a compound of Formula I-WA:



(I-WA)

wherein R_1, R_2, R_3, n, R_{14}, R_{15}, R_{16}, A, Q, X, Y, and Z are as defined above for the compounds of Formula I-WA;

or a pharmaceutically-acceptable salt thereof.

As a further embodiment, compounds of the present invention of Formulas I-WA, I-WO, I-WOHA, I-WOPC, I-WOHA, and I-WOHC, or a pharmaceutically-acceptable salt thereof as defined above and further comprise a treatment and prophylaxis of coronary artery disease and other CETP-mediated disorders in a subject, comprising administering to the subject having such disorder a therapeutically-effective amount of compounds of Formulas I-WA, I-WO, I-WOHA, I-WOPC, I-WOHA, and I-WOHC, of the present invention or a pharmaceutically-acceptable salt thereof.

Compounds of Formulas I-WA, I-WO, I-WOHA, I-WOPC, I-WOHA, and I-WOHC are capable of inhibiting activity of cholesteryl ester transfer protein (CETP), and thus could be used in the manufacture of a medicament, a method for the prophylactic or therapeutic treatment of diseases mediated by CETP, such as peripheral vascular disease, hyperlipidaemia,

hypercholesterolemia, and other diseases attributable to either high LDL and low HDL or a combination of both, or a procedure to study the mechanism of action of the cholesteryl ester transfer protein (CETP) to enable the design of better inhibitors. The compounds of Formulas I-WA, I-WO, I-WOHA, I-WOPC, I-WOHA, and I-WOHC would be also useful in prevention of cerebral vascular accident (CVA) or stroke.

Also included in the family of compounds of Formulas I-WA, I-WO, I-WOHA, I-WOPC, I-WOHA, and I-WOHC are the pharmaceutically-acceptable salts thereof. The term "pharmaceutically-acceptable salts" embraces salts commonly used to form alkali metal salts and to form addition salts of free acids or free bases. The nature of the salt is not critical, provided that it is pharmaceutically acceptable. Suitable pharmaceutically-acceptable acid addition salts of compounds of Formula I-WA may be prepared from inorganic acid or from an organic acid. Examples of such inorganic acids are hydrochloric, hydrobromic, hydroiodic, nitric, carbonic, sulfuric and phosphoric acid. Appropriate organic acids may be selected from aliphatic, cycloaliphatic, aromatic, araliphatic, heterocyclic, carboxylic and sulfonic classes of organic acids, examples of which are formic, acetic, propionic, succinic, glycolic, gluconic, lactic, malic, tartaric, citric, ascorbic, glucoronic, maleic, fumaric, pyruvic, aspartic, glutamic, benzoic, anthranilic, mesylic, salicylic, p-hydroxybenzoic, phenylacetic, mandelic, embonic (pamoic), methanesulfonic, ethylsulfonic, benzenesulfonic, sulfanilic, stearic, cyclohexylaminosulfonic, algenic, galacturonic acid. Suitable pharmaceutically-acceptable base addition salts of compounds of Formula I-WA include metallic salts made from aluminum, calcium, lithium, magnesium, potassium, sodium and zinc or organic salts made from N,N'-dibenzylethyleneldiamine, choline, chloroprocaine, diethanolamine, ethylenediamine, meglumine (N-methylglucamine) and procain. All of these salts may be prepared by conventional means from the corresponding compounds of Formulas I-WA, I-WO, I-WOHA, I-WOPC, I-WOHA, and I-WOHC by reacting, for example, the appropriate acid or base with the compounds of Formulas I-WA, I-WO, I-WOHA, I-WOPC, I-WOHA, and I-WOHC.

Also embraced within this invention is a class of pharmaceutical compositions comprising the active compounds of Formula I-WA in association with one or more non-toxic, pharmaceutically-acceptable carriers and/or diluents and/or adjuvants (collectively referred to herein as "carrier"

materials) and, if desired, other active ingredients. The active compounds of the present invention may be administered by any suitable route, preferably in the form of a pharmaceutical composition adapted to such a route, and in a dose effective for the treatment intended. The active compounds and composition may, for example, be administered orally, intravascularly, intraperitoneally, subcutaneously, intramuscularly or topically.

For oral administration, the pharmaceutical composition may be in the form of, for example, a tablet, capsule, suspension or liquid. The pharmaceutical composition is preferably made in the form of a dosage unit containing a particular amount of the active ingredient. Examples of such dosage units are tablets or capsules. The active ingredient may also be administered by injection as a composition wherein, for example, saline, dextrose or water may be used as a suitable carrier.

The amount of therapeutically active compounds which are administered and the dosage regimen for treating a disease condition with the compounds and/or compositions of this invention depends on a variety of factors, including the age, weight, sex and medical condition of the subject, the severity of the disease, the route and frequency of administration, and the particular compound employed, and thus may vary widely.

The pharmaceutical compositions may contain active ingredients in the range of about 0.1 to 2000 mg, and preferably in the range of about 0.5 to 500 mg. A daily dose of about 0.01 to 100 mg/kg body weight, and preferably between about 0.5 and about 20 mg/kg body weight, may be appropriate. The daily dose can be administered in one to four doses per day.

The compounds may be formulated in topical ointment or cream, or as a suppository, containing the active ingredients in a total amount of, for example, 0.075 to 30% w/w, preferably 0.2 to 20% w/w and most preferably 0.4 to 15% w/w. When formulated in an ointment, the active ingredients may be employed with either paraffinic or a water-miscible ointment base. Alternatively, the active ingredients may be formulated in a cream with an oil-in-water cream base. If desired, the aqueous phase of the cream base may include, for example at least 30% w/w of a polyhydric alcohol such as propylene glycol, butane-1,3-diol, mannitol, sorbitol, glycerol, polyethylene glycol and mixtures thereof. The topical formulation may desirably include a compound which enhances absorption or penetration of the active ingredient through the skin or other affected areas. Examples of such dermal penetration

enhancers include dimethylsulfoxide and related analogs. The compounds of this invention can also be administered by a transdermal device. Preferably topical administration will be accomplished using a patch either of the reservoir and porous membrane type or of a solid matrix variety. In either case, the active agent is delivered continuously from the reservoir or microcapsules through a membrane into the active agent permeable adhesive, which is in contact with the skin or mucosa of the recipient. If the active agent is absorbed through the skin, a controlled and predetermined flow of the active agent is administered to the recipient. In the case of microcapsules, the encapsulating agent may also function as the membrane.

The oily phase of the emulsions of this invention may be constituted from known ingredients in a known manner. While the phase may comprise merely an emulsifier, it may comprise a mixture of at least one emulsifier with a fat or an oil or with both a fat and an oil. Preferably, a hydrophilic emulsifier is included together with a lipophilic emulsifier which acts as a stabilizer. It is also preferred to include both an oil and a fat. Together, the emulsifier(s) with or without stabilizer(s) make-up the so-called emulsifying wax, and the wax together with the oil and fat make up the so-called emulsifying ointment base which forms the oily dispersed phase of the cream formulations. Emulsifiers and emulsion stabilizers suitable for use in the formulation of the present invention include Tween 60, Span 80, cetostearyl alcohol, myristyl alcohol, glyceryl monostearate, and sodium lauryl sulfate, among others.

The choice of suitable oils or fats for the formulation is based on achieving the desired cosmetic properties, since the solubility of the active compound in most oils likely to be used in pharmaceutical emulsion formulations is very low. Thus, the cream should preferably be a non-greasy, non-staining and washable product with suitable consistency to avoid leakage from tubes or other containers. Straight or branched chain, mono- or dibasic alkyl esters such as di-isoadipate, isocetyl stearate, propylene glycol diester of coconut fatty acids, isopropyl myristate, decyl oleate, isopropyl palmitate, butyl stearate, 2-ethylhexyl palmitate or a blend of branched chain esters may be used. These may be used alone or in combination depending on the properties required. Alternatively, high melting point lipids such as white soft paraffin and/or liquid paraffin or other mineral oils can be used.

For therapeutic purposes, the active compounds of this combination invention are ordinarily combined with one or more adjuvants appropriate to

the indicated route of administration. If administered *per os*, the compounds may be admixed with lactose, sucrose, starch powder, cellulose esters of alkanoic acids, cellulose alkyl esters, talc, stearic acid, magnesium stearate, magnesium oxide, sodium and calcium salts of phosphoric and sulfuric acids, gelatin, acacia gum, sodium alginate, polyvinylpyrrolidone, and/or polyvinyl alcohol, and then tableted or encapsulated for convenient administration. Such capsules or tablets may contain a controlled-release formulation as may be provided in a dispersion of active compound in hydroxypropylmethyl cellulose. Formulations for parenteral administration may be in the form of aqueous or non-aqueous isotonic sterile injection solutions or suspensions. These solutions and suspensions may be prepared from sterile powders or granules having one or more of the carriers or diluents mentioned for use in the formulations for oral administration. The compounds may be dissolved in water, polyethylene glycol, propylene glycol, ethanol, corn oil, cottonseed oil, peanut oil, sesame oil, benzyl alcohol, sodium chloride, and/or various buffers. Other adjuvants and modes of administration are well and widely known in the pharmaceutical art.

All mentioned references are incorporated by reference as if here written.

Although this invention has been described with respect to specific embodiments, the details of these embodiments are not to be construed as limitations.

GENERAL SYNTHETIC PROCEDURES

The compounds of the present invention can be synthesized, for example, according to the following procedures of Schemes 1 through 14 below, wherein the substituents are as defined for Formulas I-WA, I-WO, I-WOHA, I-WOPC, I-WOHA, and I-WOHC above except where further noted.

Synthetic Scheme 1 shows the preparation of compounds of formula XIIIA-H ("Secondary Heteroaryl Amines") which are intermediates in the preparation of the compounds of the present invention corresponding to Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines") wherein one substituent (A or Q) on the nitrogen is AQ-1 which can be

independently selected from the group consisting of aryl and heteroaryl, which are preferably substituted with one or more groups, and another substituent (A or Q) on the nitrogen is AQ-2 which can be independently selected from the group consisting of AQ-2 and $-CH_2(CR_{37}R_{38})_v-(CR_{33}R_{34})_u-T-(CR_{35}R_{36})_w-H$. AQ-2 and $-CH_2(CR_{37}R_{38})_v-(CR_{33}R_{34})_u-T-(CR_{35}R_{36})_w-H$ can be independently selected from the group consisting of C3-C8 alkyl, C3-C8 alkenyl, C3-C8 alkynyl, C3-C8 haloalkyl, C3-C8 haloalkenyl, C3-C6 alkoxy C1-C2 alkyl, C3-C8 hydroxyhaloalkyl, C3-C10 cycloalkyl, C5-C10 cycloalkenyl, C4-C9 saturated heterocyclyl, and C4-C9 partially saturated heterocyclyl, wherein said group may be optionally substituted.

Schemes 1 through 14, taken together, prepare tertiary heteroalkylamine compounds of the present invention by addition of a halogenated, heteroatom (for example, oxygen, sulfur, or nitrogen) containing precursor to a resulting secondary amine to introduce a heteroatom containing alkyl group wherein one of the two groups making up the secondary amine is aromatic groups and the other is aliphatic (for example, C3-C8 alkyl, C3-C8 alkenyl, C3-C8 alkynyl, C3-C8 haloalkyl, C3-C8 haloalkenyl, C3-C6 alkoxy C1-C2 alkyl, C3-C8 hydroxyhaloalkyl, C3-C10 cycloalkyl, C5-C10 cycloalkenyl), C4-C9 saturated heterocyclyl, and C4-C9 partially saturated heterocyclyl.

The "Heteroaryl Imines" corresponding to Formulas XII-AH, CXII-AH, CKXII-AH can be prepared through dehydration techniques generally known in or adaptable from the art by reacting "Heteroaryl Amine" of Formula X-AH or a "Heteroaryl Carbonyl" of Formula XI-AH with a suitable an aliphatic, saturated heterocyclic, or partially saturated heterocyclic amine or carbonyl compound as shown in Schemes 1, 3, 4, 5, 6, 12, and subsequent specific examples. For example in Scheme 3, the two reactants (AQ-2A and XI-AH) react by refluxing them in an aprotic solvent, such as hexane, toluene, cyclohexane, benzene, and the like, using a Dean-Stark type trap to remove water. After about 2-8 hours or until the removal of water is complete, the aprotic solvent is removed *in vacuo* to yield the "Heteroaryl Imine" of Formula XII-AH.

The "Secondary Cyclic Heteroaryl Amines" of Formula XIIIA-H can be prepared from the corresponding "Generic Imine" of Formula XII, "Cyclic

Heteroaryl Imine" of Formulas XII-AH, CXII-AH, and CKXII-AH can be prepared in several ways. For example, in one synthetic scheme (Reduction Method-1), the "Generic Imine" of Formula XII-AH is partially or completely dissolved in presence of a lower alcohol containing sufficient organic or mineral acid, as described in WO Patent Application No. 9738973, Swiss Patent CH 441366 and U. S. Patent Nos. 3359316 and 3334017, which are incorporated herein by reference, and then hydrogenated at 0-100°C, more preferably 20-50°C, and most preferably between 20-30°C and pressures of 10-200 psi hydrogen or more preferably between 50-70 psi hydrogen in the presence of a noble metal catalyst such as PtO_2.

In another synthetic scheme (Reduction Method-2), the "Cyclic Heteroaryl Imine" of Formulas XII-AH, CXII-AH, and CKXII-AH is slurried in a lower alcohol such as ethanol, methanol or like solvent at 0-10°C and solid sodium borohydride is added in batches over 5-10 minutes at 0-10°C with stirring. The reaction mixture is stirred below 10°C for 30-90 minutes and then is warmed gradually to 15-30°C. After about 1-10 hours, the mixture is cooled and acid is added until the aqueous layer was just acidic (pH 5-7).

In yet another synthetic scheme (Reduction Method-3), which is preferred when Z is an oxygen, the "Cyclic Heteroaryl Imine" of Formulas XII-AH, CXII-AH, and CKXII-AH is slurried in a lower alcohol solvent at 0-10°C and acidified to a pH less than 4 and sodium cyanoborohydride is added in batches over 30-90 minutes at 0-20°C with stirring and addition of a suitable organic or mineral acid to keep the pH at or below 4. The reaction mixture is stirred and warmed gradually to about 20-25°C. After about 1-10 hours, the mixture is cooled and base added until the mixture was just slightly alkaline.

The "Secondary Cyclic Heteroaryl Amines" of Formulas XIII-AH, CXIIIA-H, and CKXIII-AH can also be prepared, according to Schemes 1 and 3, by an alkylation procedure based on the nucleophilic substitution of bromides by amines. In one synthetic alkylation scheme (Alkylation Method-1), a "Cyclic Amine" of Formula AQ-2A or a "Generic Amine-1" of Formula X is reacted with a "Heteroaryl Bromide" of Formula XXI-AH or "Generic

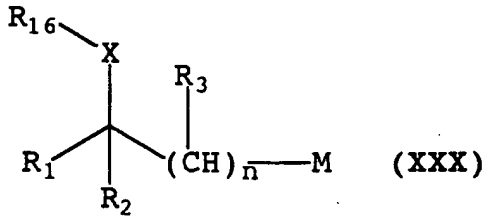
Bromide" of Formula XXI as described in Vogel's Textbook of Practical Organic Chemistry, Fifth Edition, 1989, pages 902 to 905 and references cited therein all of which are incorporated herein by reference. In an alternate synthetic alkylation scheme exemplified in Scheme 1, an "Amine" of Formula XXII is reacted with a "Heteroaryl Bromide" in a method employing palladium catalyzed carbon-nitrogen bond formation. Suitable procedures for this conversion are described in Wagaw and Buchwald, J. Org. Chem.(1996), 61, 7240-7241, Wolfe, Wagaw and Buchwald, J. Am. Chem. Soc. (1996), 118, 7215-7216, and Wolfe and Buchwald, Tetrahedron Letters (1997), 38(36), 6359-6362 and references cited therein all of which are incorporated herein by reference.

The "Generic Secondary Amine", "Heteroaryl Amine", "Cyclic Amine", "Alicyclic Amine", and "Heteoaryl Hydroxylamine" amines and hydroxylamines, the "Generic Carbonyl", "Heteroaryl Carbonyl", "Cyclic Carbonyl", and "Cyclic Ketone" aldehydes and ketones, and "Generic Bromide-1", Generic Bromide-2", "Heteroaryl Bromide", and the like halides, tosylates, mesylates, triflates, and precursor alcohols required to prepare the "Secondary Cyclic Heteroaryl Amine" compounds are available from commercial sources or can be prepared by one skilled in the art from published procedures. Commercial sources include but are not limited to Aldrich Chemical, TCI-America, Lancaster-Synthesis, Oakwood Products, Acros Organics, and Maybridge Chemical. Disclosed procedures for "Generic Amine" amines, hydroxylamines, and hydrazines include Sheradsky and Nov, J. Chem. Soc., Perkin Trans.1 (1980), (12), 2781-6; Marcoux, Doye, and Buchwald, J. Am. Chem. Soc. (1997), 119, 1053-9; Sternbach and Jamison, Tetrahedron Lett. (1981), 22(35), 3331-4; U. S. Patent No. 5306718; EP No. 314435; WO No. 9001874; WO No. 9002113; JP No. 05320117; WO No. 9738973; Swiss Patent No. CH 441366; U. S. Patents Nos. 3359316 and 3334017; and references cited therein which are incorporated herein by reference.

Synthetic Schemes 2, 10 and 11 show the preparation of the class of compounds of the present invention corresponding to Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines").

Derivatives of "Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols" or "Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines", in which the

heteroatom (O, N, or S) is attached to an alkyl group removed from the amine by two or more carbons are readily prepared by anion chemistry using the method of Scheme 2. The anion of "Secondary Amine" amines and hydroxylamines of Formula XIII are readily formed by dissolving the specific amine, hydroxylamine, or hydrazine in an aprotic solvent, such as tetrahydrofuran, toluene, ether, dimethylformamide, and dimethylformamide, under anhydrous conditions. The solution is cooled to a temperature between -78 and 0°C, preferably between -78 and -60°C and the anion formed by the addition of at least one equivalent of a strong, aprotic, non-nucleophillic base such as NaH or n-butyllithium under an inert atmosphere for each acidic group present. Maintaining the temperature between -78 and 0°C, preferably between -78 and -60°C, with suitable cooling, an appropriate alkyl halide, alkyl benzenesulfonate such as a alkyl tosylate, alkyl mesylate, alkyl triflate or similar alkylating reagent of the general structure:

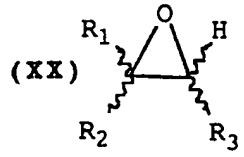


(XXX)

where m is zero, X can be RN, O, and S, and M is a readily displaceable group such as chloride, bromide, iodide, tosylate, triflate, and mesylate. After allowing the reaction mixture to warm to room temperature, the reaction product is added to water, neutralized if necessary, and extracted with a water-immiscible solvent such as diethyl ether or methylene chloride. The combined aprotic solvent extract is washed with saturated brine, dried over drying agent such as anhydrous $MgSO_4$ and concentrated *in vacuo* to yield crude Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines"). This material is purified, for example, by eluting through silica gel with a medium polar solvent such as ethyl acetate in a non-polar solvent such as hexanes to yield purified Formula I-WA and Formula I-WO. Products are structurally confirmed by low and high resolution mass spectrometry and NMR.

Compounds of Formula (XXX), which can be used to prepare I-WA, I-WO, I-WOPA, I-WOPC, I-WOHA, and I-WOHC, are given in Table 2. Reagents 1a and 2a in Table 2 are prepared from the corresponding alcohols. The tosylates are readily obtained by reacting the corresponding alcohol with tosyl chloride using procedures found in House's Modern Synthetic Reactions, Chapter 7, W. A. Benjamin, Inc., Shriner, Fuson, and Curtin in The Systematic Indentification of Organic Compounds, 5th Edition, John Wiley & Sons, and Fieser and Fieser in Reagents for Organic Synthesis, Volume 1, John Wiley & Sons, which are incorporated herein by reference.

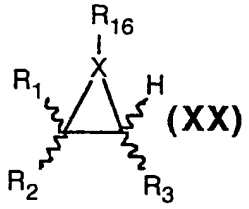
A preferred procedure for Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines" compounds is Method A of Schemes 2, 10, 11, and 14. Oxirane reagents useful in Method A are exemplified, but not limited to those in Table 1. Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl 1-Amino-2-alcohol") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary 2-Heteroalkylamine") compounds are prepared by using "Secondary Cyclic Heteroaryl Amine" and "Alicyclic Heteroaryl Amine" amines and hydroxylamines of Formulas XIIIA-H, CXIIIA-H, CKXIII-AH, ACXIIIA-H, and RACXIIIA-H prepared above with oxiranes of the type listed in Table 1 and represented by the general structure:



In some cases, the oxiranes are prepared by reaction of epoxidation reagents such as MCPBA and similar type reagents readily selectable by a person of skill-in-the-art with alkenes. Fieser and Fieser in Reagents for Organic Synthesis, John Wiley & Sons provides, along with cited references, numerous suitable epoxidation reagents and reaction conditions, which are incorporated herein by reference.

Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary 2-Heteroalkylamine") compounds, wherein the 2-hetero group is an amino, substituted amino, or thiol, can be prepared by using appropriate aziridines and thiiranes according to Method A of Scheme 2. Aziridine and thiirane reagents

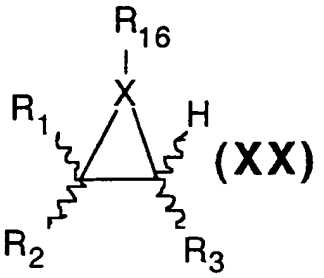
useful in Method A are exemplified, but not limited to those in Table 1. These Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary 2-Heteroalkylamine") compounds, wherein the 2-hetero group is an amino, substituted amino, or thiol, can be prepared by using "Secondary Cyclic Heteroaryl Amine" and "Alicyclic Heteroaryl Amine" amines and hydroxylamines of Formulas XIIIA-H, CXIIIA-H, CKXIII-AH, ACXIIIA-H, and RACXIIIA-H prepared above with aziridines and thiiranes of the type listed in Table 1 and represented by the general structure:



(XX)

wherein X is selected from N and S and R_{16} is hydrogen or another suitable group when X is N.

Table 1. Structure of Oxirane, Aziridine, and Thiirane Reagents.



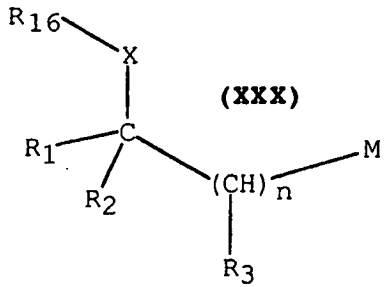
(XX)

Rgnt No.	R_{16}	X	R_1	R_2	R_3
1	------	O	CF_3	H	H
2	------	O	CCl_3	H	H
3	------	O	CF_3	CH_3	H
4	------	O	CF_3CF_2	H	H
5	------	O	$CF_3CF_2CF_2$	H	H
6	------	O	$CF_3OCF_2CF_2$	H	H
7	------	O	CF_3CH_2	H	H
8	------	O	CF_3	CHF_2	H
9	------	O	CF_3	H	CF_3
10	------	O	CF_3	CF_3	H
11	------	O	CF_3	C_6H_5	H
12	------	O	CCl_3	C_6H_5	H
13	------	O	CCl_3	Cyclopropyl	H
14	------	O	CCl_3	CH_3	H
15	------	O	CCl_3	$(CH_3)_2CH$	H
16	------	O	$CHCl_2$	H	H
17	------	O	$CHCl_2$	Cl	H
18	------	O	CF_3	H	CH_3
19	H	N	CF_3	CF_3	H

Table 1. (continued) Structure of Oxirane, Aziridine, and Thiirane Reagents.

Rgnt No.	R_{16}	X	R_1	R_2	R_3
20	H	N	CF_3	H	H
21	Benzyl	N	CF_3	H	H
22	CH_3O	N	CF_3	H	H
23	CH_3	N	CF_3	H	H
24	Benzyloxy	N	CF_3	H	H
25	------	S	CF_3	H	H
26	------	S	CF_3CF_2	H	H
27	------	O	CCl_3CH_2	H	H
28	------	O	CBr_3CH_2	H	H
29	------	O	$CHBr_2CH_2$	H	H
30	------	O	$CBrCl_2$	H	H
31	------	O	$CClF_2$	H	H
32	------	O	CCl_2F	H	H
33	------	O	CCl_3CCl_2	H	H
43	------	O	FCH_2	H	H
46	------	O	CF_3	$R_2+R_3 = (CH_2)_3$	
47	------	O	CF_3	$R_2+R_3 = (CH_2)_4$	
48	------	O	CHF_2	$R_2+R_3 = (CH_2)_4$	
56	------	O	$CBrF_2CClFCH_2$	H	H
57	------	O	$HCF_2CF_2OCH_2$	H	H

Table 2. Structure and Source of Alcohol and Glycol Reagents.



Reagent Number	R_1	n	M	R_2	R_3	X-R_{16}	Source of Reagent
1A	CF_3	3	OTs	H	H	OH	Chiral separation and then tosylation of alcohol from Justus Liebigs Ann. Chem. (1969), 720, 81-97.
2A	$CF_3CH_2CH_2$	3	OTs	H	H	OH	Chiral separation and then tosylation of alcohol from Z. Naturforsch., B: Chem. Sci. (1997), 52 (3). 413-418

A mixture of a "Secondary Amine" amine or hydroxylamine and an oxirane of Formula XX are stirred and heated to 40-90°C for 5 to 48 hours in a tightly capped or contained reaction vessel. A Lewis acid such as ytterbium triflate in acetonitrile may be added to speed up reaction and improve yield. When a Lewis acid is used, the reaction should be carried out under inert, anhydrous conditions using a blanket of dry nitrogen or argon gas. After cooling to room temperature and testing the reaction mixture for complete reaction by thin layer chromatography or high pressure liquid chromatography (hplc), the reaction product is added to water and extracted with a water immiscible solvent such as diethyl ether or methylene chloride. (Note: If the above analysis indicates that reaction is incomplete, heating should be resumed until complete with the optional addition of more of the oxirane). The combined aprotic solvent extract is washed with saturated brine, dried over drying agent such as anhydrous $MgSO_4$ and concentrated *in vacuo* to yield crude Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines") compounds. This material is purified by eluting through silica gel with 5-40% of a medium polar solvent such as ethyl acetate in a non-polar solvent such as hexanes to yield the Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines") compounds. Products are tested for purity by HPLC. If necessary, the Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines") compounds are purified by additional chromatography or recrystallization. Products are structurally confirmed by low and high resolution mass spectrometry and NMR. Examples of specific Formula VII Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines") prepared are summarized in the Examples and Example Tables 1 through 7.

Specific Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines") analogs of the Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines") compounds summarized in the Examples and Example Tables 1 through 7, wherein the hydroxyl or oxy group are replaced with an amino, substituted amino, aza, or thiol, can be prepared by

using the appropriate aziridine reagents or thiirane reagents readily by adapting the procedures in the numerous specific **Examples** and **Schemes** disclosed in the present invention. Similarly, intermediates, in which the hydroxyl or oxy group of said intermediates are replaced with an amino, substituted amino, aza, or thiol, can be converted using the numerous specific **Examples** and **Schemes** disclosed in the present invention to other Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines") compounds.

Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines") compounds can further be prepared in an alternate manner to procedures disclosed above and in Schemes 1, 2, and 3. Schemes 12 and 13 detail such procedures to prepare compounds of the present invention by initial formation of an halogenated, oxygen containing primary alkylamine XL ("Generic Substituted Alkylamine"). Said halogenated, oxygen containing primary alkylamine XL, formed in Scheme 12, is itself converted to secondary amine LX-H ("Heteroaryl Alkyl Amine) using procedures disclosed above. Primary alkylamine XL is first reacted with an aldehydic or ketonic carbonyl compound, XI-AH ("Heteroaryl Carbonyl") with azeotropic distillation to form imines, L-H ("Heteroaryl Imine"). Said imine L-H are then reduced with or without prior isolation by Reduction Methods 1, 2 or 3 as disclosed above and in Scheme 1 to yield secondary amines LX-H ("Heteroaryl Alkyl Amine). Said secondary amine LX-H can be converted according to Scheme 14 to Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols").

Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines") compounds can further be prepared in an alternate manner to procedures disclosed above and in additional Schemes.

Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") are alternately referred to as Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl 2-hydroxyalkylamines").

Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines") compounds can themselves serve as intermediates for conversion to additional compounds of this invention. Compounds of the present invention useful as intermediates include those in which the R_5 or R_7 position substituent in

Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines") compounds is a bromo group, hydroxyl group, sulfhydryl group, bromomethyl or other bromoalkyl groups, nitro group, amino group, methoxy carbonyl or other alkoxy carbonyl groups, cyano group, or acyl groups. Other preferred compounds of the present invention useful as intermediates include those in which the R_{10} position substituent in Formulas I-WA or I-WO is a bromo group, hydroxyl group, sulfhydryl group, bromomethyl or other bromoalkyl groups, nitro group, amino group, methoxy carbonyl or other alkoxy carbonyl groups, cyano group, or acyl groups. Other compounds of Formulas I-WA or I-WO and the present invention useful as intermediates include those in which one or more of R_6, R_{11}, and R_{12} substituents in Formulas I-WA or I-WO is a bromo group, hydroxyl group, sulfhydryl group, bromomethyl or other bromoalkyl groups, nitro group, amino group, methoxy carbonyl or other alkoxy carbonyl groups, cyano group, or acyl groups.

Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") are alternately referred to as Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Tertiary 2-hydroxyalkylamines").

A 3-bromo substituent at the R_5 position in Formula I-WO ("Alicyclic/Cyclic 3-Bromoaryl Tertiary 2-Hydroxyalkylamines") can be reacted with a phenol to afford 3-phenoxy compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-Phenoxyaryl Tertiary 2-Hydroxyalkylamines").

A 3-bromo substituent at the R_5 position in Formula I-WO ("Alicyclic/Cyclic 3-Bromoheteroaryl Tertiary 2-hydroxyalkylamine") can, be reacted, for example, with a phenol to afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-Aryloxyaryl, 3-Heteroaryloxyaryl, 3-Heteroaryloxyheteroaryl, and 3-Aryloxyheteroaryl Tertiary 2-Hydroxyalkylamines").

A 3-bromo substituent at the R_5 position in Formula I-WO ("Alicyclic/Cyclic 3-Bromoaryl Tertiary 2-hydroxyalkylamine") can be reacted with a phenol to afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-Phenylaryl Tertiary 2-Hydroxyalkylamine").

Conversion of a 3-bromo substituent at the R_5 position in Formula I-WO ("Alicyclic/Cyclic 3-Bromoaryl Tertiary 2-hydroxyalkylamine") by reaction with a primary or secondary amine can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3- R_{22}aminoaryl Tertiary 2-Hydroxyalkylamine").

Conversion of a 3-bromo substituent at the R_5 position in Formula I-WO ("Alicyclic/Cyclic 3-Bromoaryl Tertiary 2-hydroxyalkylamine") by reaction with an aryl borinate can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-Phenylaryl Tertiary 2-Hydroxyalkylamine").

Conversion of a 3-bromo substituent at the R_5 position in Formula I-WO ("Alicyclic/Cyclic 3-Bromoaryl Tertiary 2-hydroxyalkylamine") by reaction with a heteroaryl dibutyl tin compound can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-Heteroarylaryl Tertiary 2-Hydroxyalkylamine").

Conversion of a 3-bromomethyl substituent at the R_5 position in Formula I-WO ("Alicyclic/Cyclic 3-Bromomethylaryl Tertiary 2-hydroxyalkylamine") by reaction with an aryl borinate can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-Arylmethylaryl Tertiary 2-Hydroxyalkylamine").

Conversion of a 3-hydroxyl substituent at the R_5 position in Formula I-WO ("Alicyclic/Cyclic 3-Hydroxyheteroaryl Tertiary 2-hydroxyalkylamine") by reaction with an aryl bromide or heteroaryl bromide can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-Aryloxyaryl, 3-Heteroaryloxyaryl, 3-Heteroaryloxyheteroaryl, and 3-Aryloxyheteroaryl Tertiary 2-Hydroxyalkylamines").

Conversion of a 3-hydroxyl substituent at the R_5 position in Formula I-WO ("Alicyclic/Cyclic 3-Hydroxyaryl Tertiary 2-hydroxyalkylamine") by reaction with an aryl bromide can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-Phenoxyaryl Tertiary 2-Hydroxyalkylamine").

Conversion of a 3-hydroxyl substituent at the R_5 position in Formula I-WO ("Alicyclic/Cyclic 3-Hydroxyheteroaryl Tertiary 2-hydroxyalkylamine") by reaction with an aralkyl bromide or heteroaralkyl bromide can afford

additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-Aralkyloxyaryl, 3-Heteroaralkyloxyaryl, 3-Heteroaralkyloxyheteroaryl, and 3-Aralkyloxyheteroaryl Tertiary 2-Hydroxyalkylamines").

Conversion of a 3-hydroxyl substituent at the R_5 position in Formula I-WO ("Alicyclic/Cyclic 3-Hydroxyaryl Tertiary 2-hydroxyalkylamine") by reaction with an aralkyl bromide can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-Aralkyloxyaryl Tertiary 2-Hydroxyalkylamine").

Conversion of a 3-hydroxyl substituent at the R_5 position in Formula I-WO ("Alicyclic/Cyclic Polycyclic 3-Hydroxyaryl Tertiary 2-hydroxyalkylamine") by reaction with a displaceable organo bromide can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-Organooxyaryl Tertiary 2-Hydroxyalkylamine").

Conversion of a 3-thio substituent at the R_5 position in Formula I-WO ("Alicyclic/Cyclic 3-thioaryl Tertiary 2-hydroxyalkylamine") by reaction with a displaceable organo bromide can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-Organothiaaryl Tertiary 2-Hydroxyalkylamine"). "Alicyclic/Cyclic 3-Organothiaaryl Tertiary 2-Hydroxyalkylamines" can be oxidized to sulfonyl compounds of 3-Organosulfonylaryl Tertiary 2-Hydroxyalkylamine").

Conversion of a 3-nitro substituent at the R_5 position in Formula I-WO ("Alicyclic/Cyclic 3-Nitroaryl Tertiary 2-hydroxyalkylamine") by hydrogenation can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-Aminoaryl Tertiary 2-Hydroxyalkylamine"). Formula I-WO ("Alicyclic/Cyclic 3-Aminoaryl Tertiary 2-Hydroxyalkylamines") can be acylated to acyl amide compounds of Formula I-WO ("Alicyclic/Cyclic 3-Acylaminoaryl Tertiary 2-Hydroxyalkylamine").

Conversion of a 3-amino substituent at the R_5 position in Formula I-WO ("Alicyclic/Cyclic 3-Aminoaryl Tertiary 2-hydroxyalkylamine") by reaction with carbonyl compounds can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-(Saturated Nitrogen Heterocycl-1yl)aryl Tertiary 2-Hydroxyalkylamine" and "Alicyclic/Cyclic 3-(Unsaturated Nitrogen Heterocycl-1yl)aryl Tertiary 2-Hydroxyalkylamine").

Conversion of a 3-methoxycarbonyl substituent at the R_5 position in Formula I-WO ("Alicyclic/Cyclic 3-Carbomethoxyaryl Tertiary 2-hydroxyalkylamine") by reaction with amination reagents can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-Carboxamidoaryl Tertiary 2-Hydroxyalkylamine").

Conversion of a 3-cyano substituent at the R_5 position in Formula I-WO ("Alicyclic/Cyclic 3-Cyanoaryl Tertiary 2-hydroxyalkylamine") by reaction with organometallic reagents can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-Acylaryl Tertiary 2-Hydroxyalkylamine"). Said "Alicyclic/Cyclic 3-Acylaryl Tertiary 2-Hydroxyalkylamines", can be reduced to hydroxyl compounds of Formula I-WO ("Alicyclic/Cyclic 3-Hydroxysubstitutedmethylaryl Tertiary 2-Hydroxyalkylamine").

Conversion of a 3-methoxycarbonyl substituent at the R_{10} position in Formula I-WO ("Alicyclic/Cyclic 3-Carbomethoxyaryl Tertiary 2-hydroxyalkylamine") by reaction with amination reagents can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-Carboxamidoaryl Tertiary 2-Hydroxyalkylamine").

Conversion of a 3-methoxycarbonyl substituent at the R_{10} position in Formula I-WO ("Alicyclic/Cyclic 3-Carbomethoxyaryl Tertiary 2-hydroxyalkylamine") by reaction with an organometallic reagent can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-(bis-Organohydroxymethyl)aryl Tertiary 2-Hydroxyalkylamine").

Conversion of a 3-methoxycarbonyl substituent at the R_{10} position in Formula I-WO ("Alicyclic/Cyclic 3-Carbomethoxyaryl Tertiary 2-hydroxyalkylamine") by reaction with lithium aluminum hydride can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-Hydroxymethylaryl Tertiary 2-Hydroxyalkylamine").

Conversion of a 3-methoxycarbonyl substituent at the R_{10} position in Formula I-WO ("Alicyclic/Cyclic 3-Carbomethoxyaryl Tertiary 2-hydroxyalkylamine") by reaction with an alkylation reagent can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-(bis-Organo-hydroxymethyl)aryl Tertiary 2-Hydroxyalkylamine").

Conversion of a 3-methoxycarbonyl substituent at the R_{10} position in Formula I-WO ("Alicyclic/Cyclic 3-Carbomethoxyaryl Tertiary 2-hydroxyalkylamine") by reaction intially with an amidation reagent and then an organometallic reagent can afford additional compounds of the present invention of Formula I-WO ("Alicyclic/Cyclic 3-(Organo-carbonyl)aryl Tertiary 2-Hydroxyalkylamine").

Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines") and other compounds of this invention posssessing hydroxyl, thiol, and amine functional groups can be converted to a wide variety derivatives. The hydroxyl group X, wherein R_{16} is a hydrogen, of compounds of the present invention can be readily converted to esters of carboxylic, sulfonic, carbamic, phosphonic, and phosphoric acids. Acylation to form a carboxylic acid ester is readily effected using a suitable acylating reagent such as an aliphatic acid anhydride or acid chloride. The corresponding aryl and heteroaryl acid anhydrides and acid chlorides can also be used. Such reactions are generally carried out using an amine catalyst such as pyridine in an inert solvent. In like manner, compounds that have at least one hydroxyl group present in the form of an alcohol or phenol can be acylated to its corresponding esters. Similarly, carbamic acid esters (urethans) can be obtained by reacting any hydroxyl group with isocyanates and carbamoyl chlorides. Sulfonate, phosphonate, and phosphate esters can be prepared using the corresponding acid chloride and similar reagents. Compounds that have at least one thiol group present can be converted to the corresponding thioesters derivatives analogous to those of alcohols and phenols using the same reagents and comparable reaction conditions. Compounds of Formulas I-WA, I-WO, and other compounds of the present invention that have at least one primary or secondary amine group present can be converted to the corresponding amide derivatives. Amides of carboxylic acids can be prepared using the appropriate acid chloride or anhydrides with reaction conditions analogous to those used with alcohols and phenols. Ureas of the corresponding primary or secondary amine can be prepared using isocyanates directly and carbamoyl chlorides in the presence of an acid scavenger such as triethylamine or pyridine. Sulfonamides can be prepared from the corresponding sulfonyl chloride in the presence of aqueous sodium hydroxide. Suitable procedures and methods for preparing these derivatives can be found in House's Modern Synthetic Reactions, W. A.

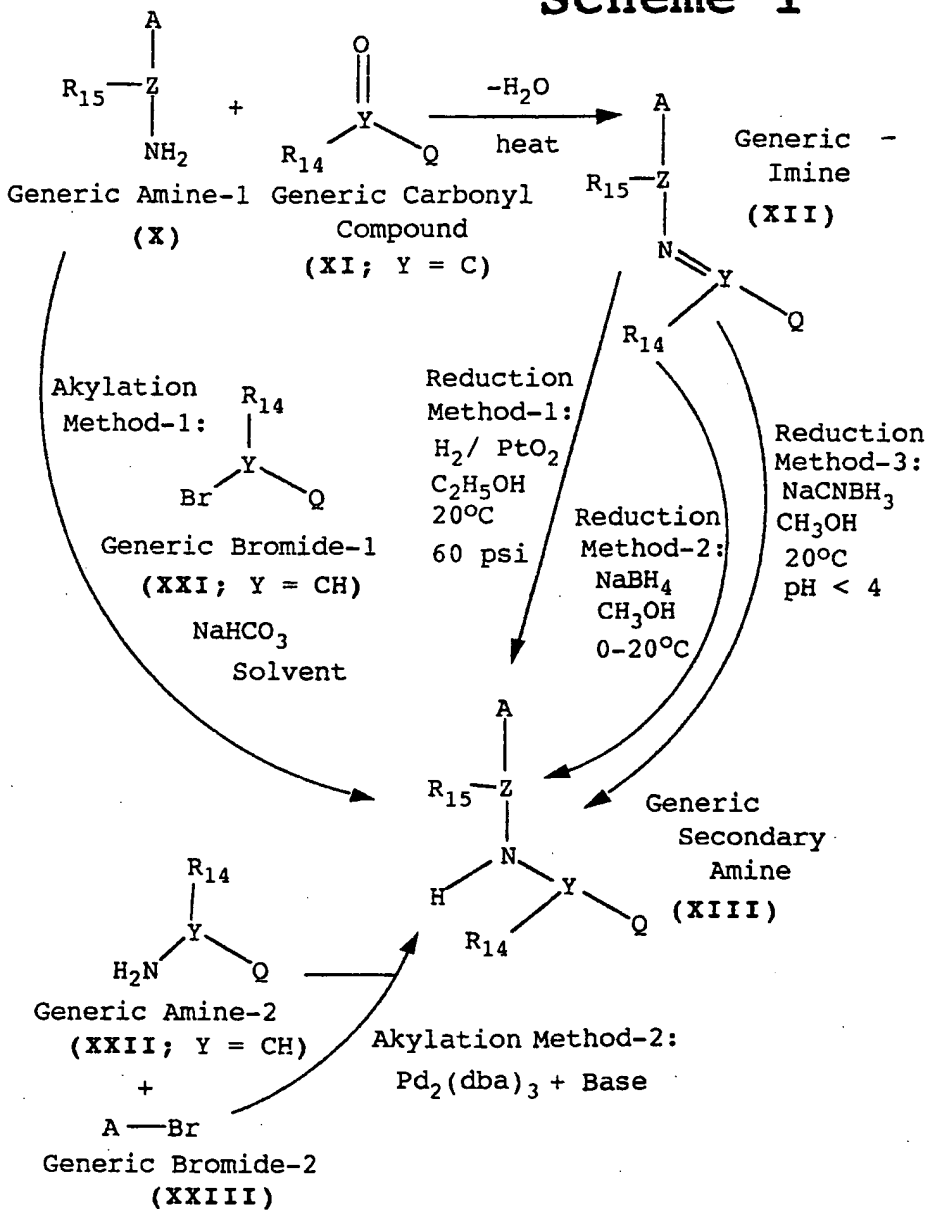
Benjamin, Inc., Shriner, Fuson, and Curtin in The Systematic Indentification of Organic Compounds, 5th Edition, John Wiley & Sons, and Fieser and Fieser in Reagents for Organic Synthesis, Volume 1, John Wiley & Sons. Reagents of a wide variety that can be used to derivatize hydroxyl, thiol, and amines of compounds of Formulas I-WA, I-WO, and other compounds of the present invention are available from commerical sources or the references cited above, which are incorporated herein by reference.

Formula I-WO ("Alicyclic/Cyclic Aryl/Heteroaryl Aminoalcohols") and Formula I-WA ("Alicyclic/Cyclic Aryl/Heteroaryl tertiary Heteroalkylamines") and other compounds of this invention posssessing hydroxyl, thiol, and amine functional groups can be alkylated to a wide variety derivatives. The hydroxyl group X, wherein R_{16} is a hydrogen, of compounds of Formulas I-WA, I-WO, and other compounds of the present invention can be readily converted to ethers. Alkylation to form an ether is readily effected using a suitable alkylating reagent such as an alkyl bromide, alkyl iodide or alkyl sulfonate. The corresponding aralkyl, heteroaralkyl, alkoxyalkyl, aralkyloxyalkyl, and heteroaralkyloxyalkyl bromides, iodides, and sulfonates can also be used. Such reactions are generally carried out using an alkoxide forming reagent such as sodium hydride, potassium t-butoxide, sodium amide, lithium amide, and n-butyl lithium using an inert polar solvent such as DMF, DMSO, THF, and similar, comparable solvents. amine catalyst such as pyridine in an inert solvent. In like manner, compounds of Formulas I-WA, I-WO, and the like that have at least one hydroxyl group present in the form of an alcohol or phenol can be alkylated to their corresponding ethers. Compounds of Formulas I-WA, I-WO, and other compounds that have at least one thiol group present can be converted to the corresponding thioether derivatives analogous to those of alcohols and phenols using the same reagents and comparable reaction conditions. Compounds of Formulas I-WA, I-WO, and other compounds that have at least one primary, secondary or tertiary amine group present can be converted to the corresponding quaternary ammonium derivatives. Quaternary ammonium derivatives can be prepared using the appropriate bromides, iodides, and sulfonates analogous to those used with alcohols and phenols. Conditions involve reaction of the amine by warming it with the alkylating reagent with a stoichiometric amount of the amine (i.e., one equivalent with a tertiary amine, two with a secondary, and three with a primary). With primary and secondary amines, two and one equivalents, respectively, of an acid

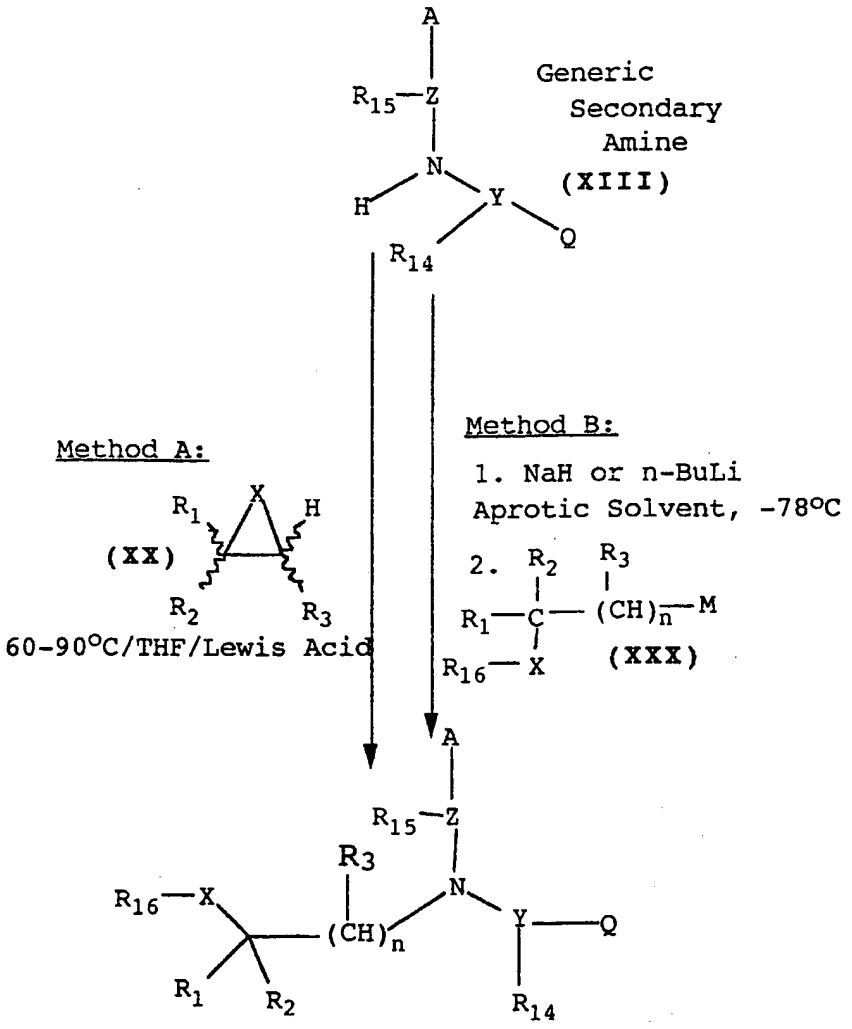
scavenger are used concurrently. Tertiary amines can be prepared from the corresponding primary or secondary amine by reductive alkylation with aldehydes and ketones using reduction methods 1, 2, or 3 as shown in Scheme 1. Suitable procedures and methods for preparing these derivatives can be found in House's Modern Synthetic Reactions, W. A. Benjamin, Inc., Shriner, Fuson, and Curtin in The Systematic Indentification of Organic Compounds, 5th Edition, John Wiley & Sons, and Fieser and Fieser in Reagents for Organic Synthesis, Volume 1, John Wiley & Sons. Perfluoroalkyl derivatives can be prepared as described by DesMarteau in J. Chem. Soc. Chem. Commun. 2241 (1998). Reagents of a wide variety that can be used to derivatize hydroxyl, thiol, and amines of compounds of Formulas I-WA, I-WO, and the like are available from commerical sources or the references cited above, which are incorporated herein by reference.

The following examples are provided to illustrate the present invention and are not intended to limit the scope thereof. Those skilled in the art will readily understand that known variations of the conditions and processes of the following preparative procedures can be used to prepare these compounds.

Scheme 1

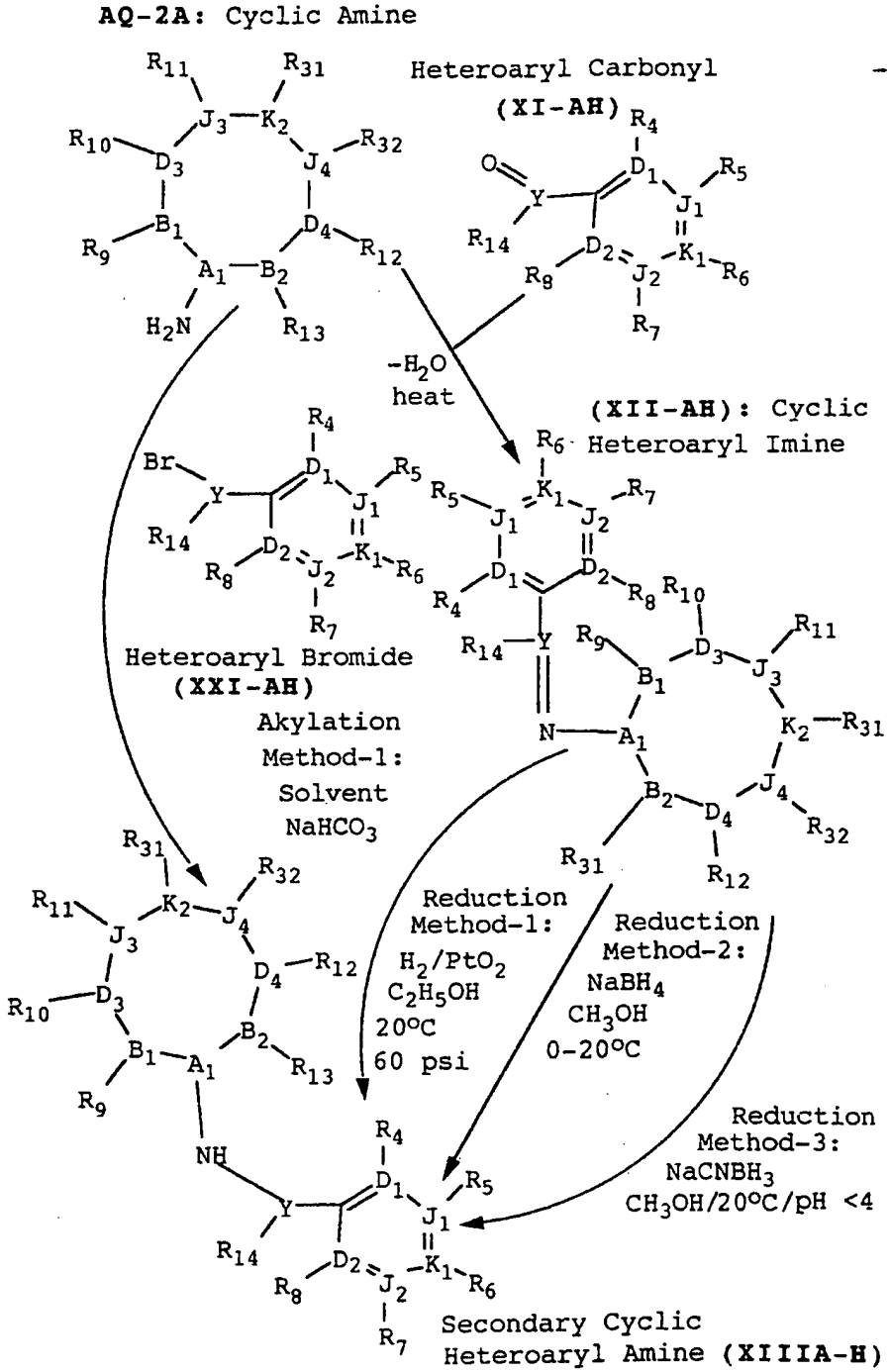

Generic Amine-1
(X)
Generic Carbonyl Compound
(XI; Y = C)
-H2O
heat
Generic Imine
(XII)
Akylation Method-1:
Generic Bromide-1
(XXI; Y = CH)
NaHCO3
Solvent
Reduction Method-1:
H2/ PtO2
C2H5OH
20°C
60 psi
Reduction Method-2:
NaBH4
CH3OH
0-20°C
Reduction Method-3:
NaCNBH3
CH3OH
20°C
pH < 4
Generic Secondary Amine
(XIII)
Generic Amine-2
(XXII; Y = CH)
+
Generic Bromide-2
(XXIII)
Akylation Method-2:
Pd2(dba)3 + Base

Scheme 2

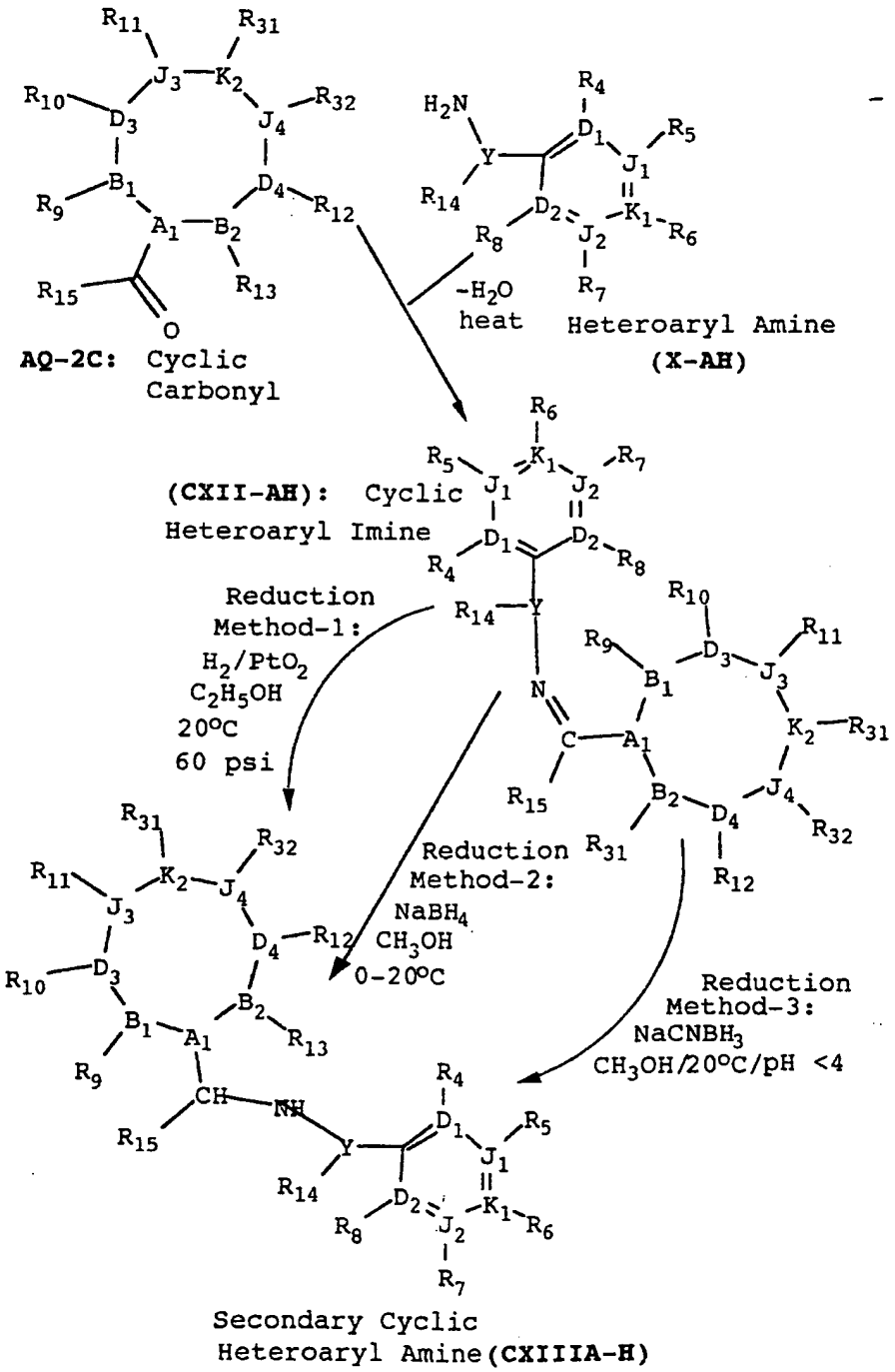


I-WA (X = O, S, NH), **I-WO**, **I-WOPA**, **I-WOPC**, **I-WOHA**, and **I-WOHC** (X = O in others)

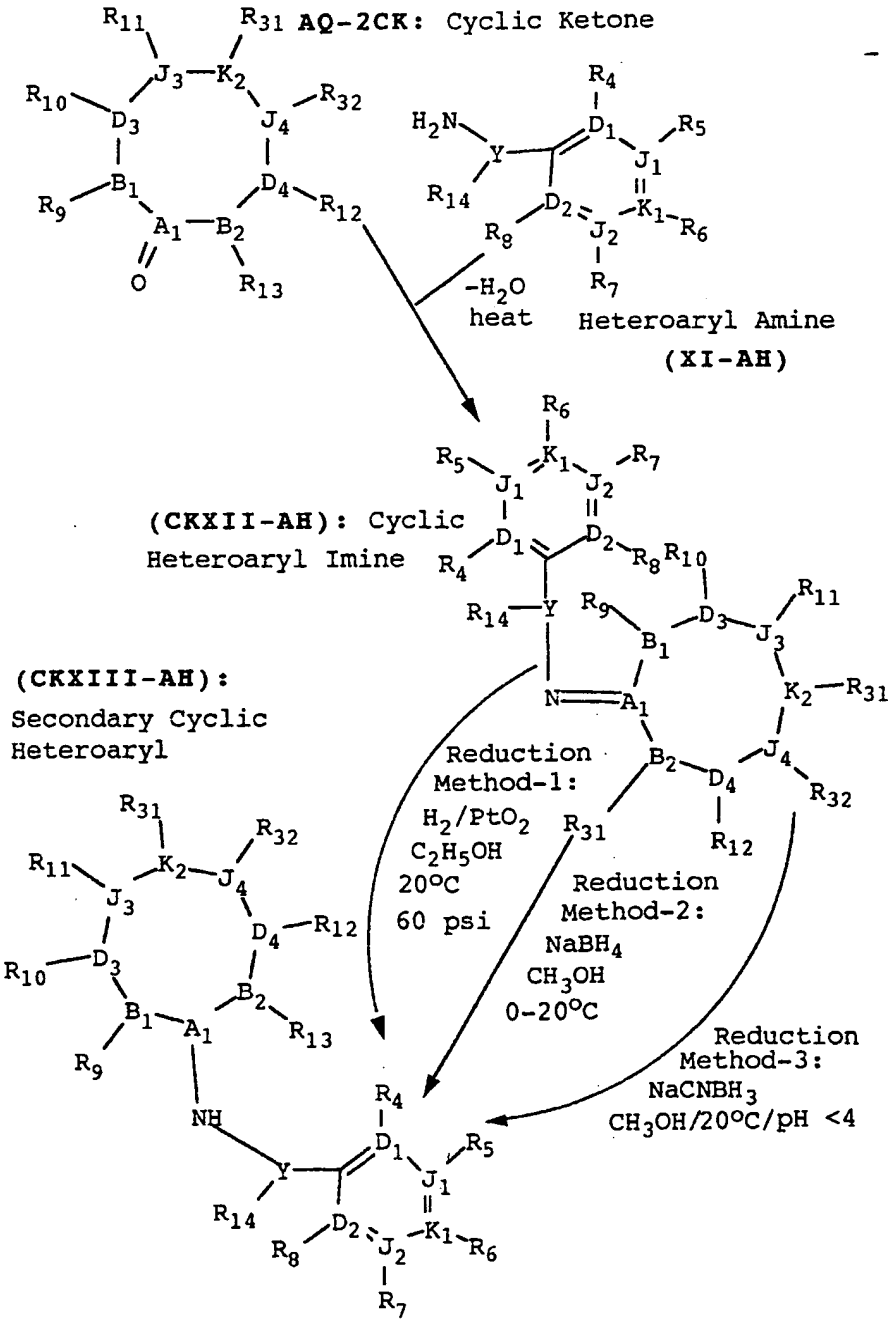
Scheme 3


AQ-2A: Cyclic Amine
Heteroaryl Carbonyl
(XI-AH)
-H2O
heat
(XII-AH): Cyclic
Heteroaryl Imine
Heteroaryl Bromide
(XXI-AH)
Akylation
Method-1:
Solvent
NaHCO3
Reduction
Method-1:
H2/PtO2
C2H5OH
20°C
60 psi
Reduction
Method-2:
NaBH4
CH3OH
0-20°C
Reduction
Method-3:
NaCNBH3
CH3OH/20°C/pH <4
Secondary Cyclic
Heteroaryl Amine (XIIIA-H)

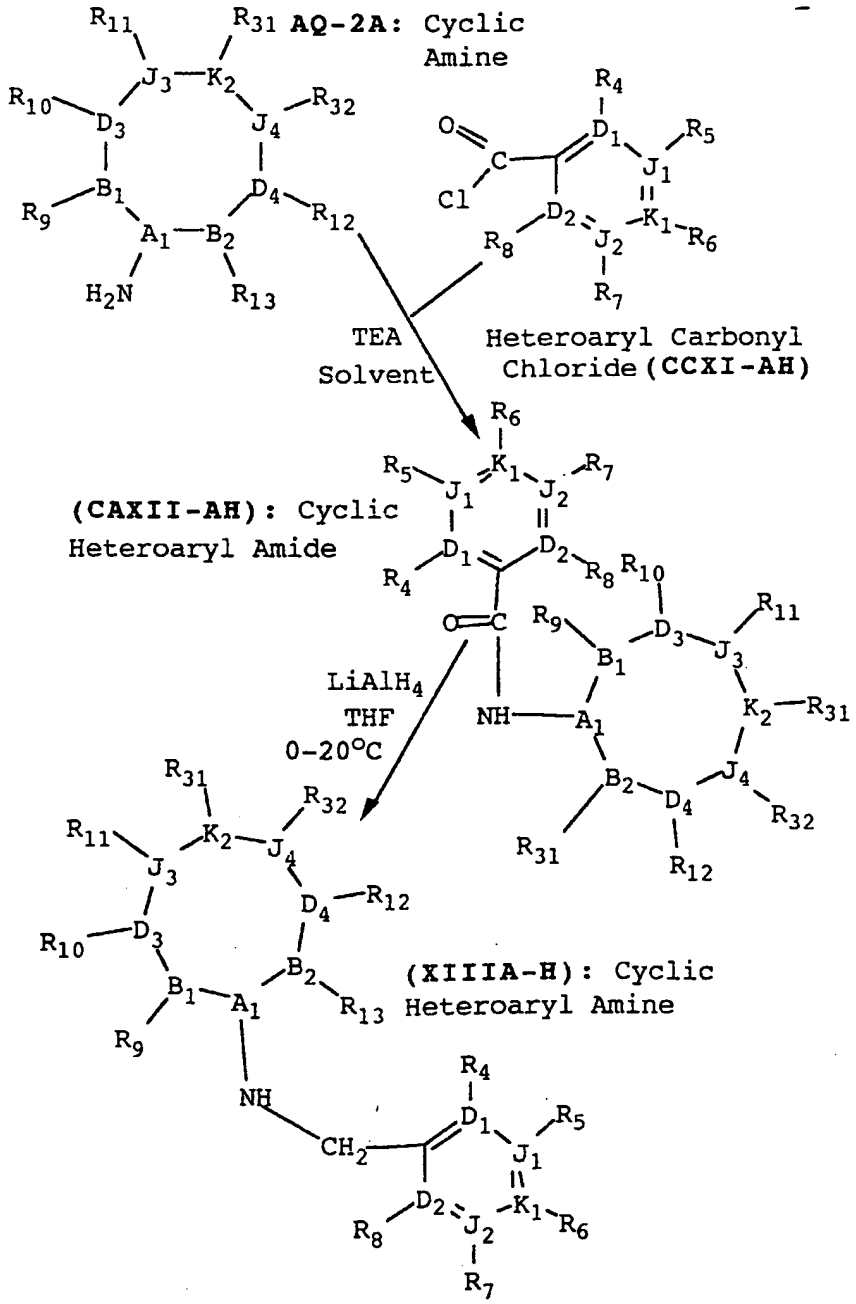
Scheme 4


AQ-2C: Cyclic Carbonyl
-H2O
heat
Heteroaryl Amine (X-AH)
(CXII-AH): Cyclic Heteroaryl Imine
Reduction Method-1:
H2/PtO2
C2H5OH
20°C
60 psi
Reduction Method-2:
NaBH4
CH3OH
0-20°C
Reduction Method-3:
NaCNBH3
CH3OH/20°C/pH <4
Secondary Cyclic Heteroaryl Amine (CXIIIA-H)

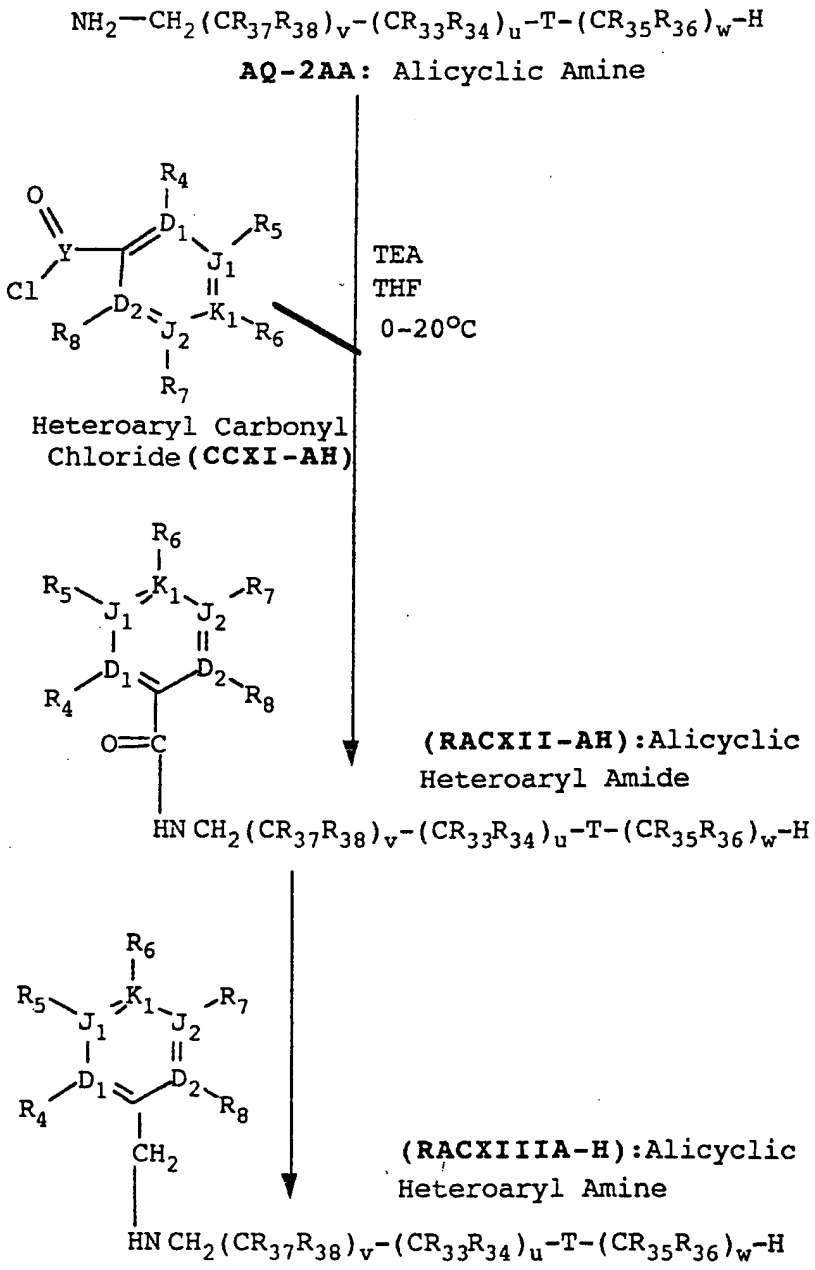
Scheme 5


AQ-2CK: Cyclic Ketone
Heteroaryl Amine
(XI-AH)
-H2O
heat
(CKXII-AH): Cyclic
Heteroaryl Imine
(CKXIII-AH):
Secondary Cyclic
Heteroaryl
Reduction
Method-1:
H2/PtO2
C2H5OH
20°C
60 psi
Reduction
Method-2:
NaBH4
CH3OH
0-20°C
Reduction
Method-3:
NaCNBH3
CH3OH/20°C/pH <4

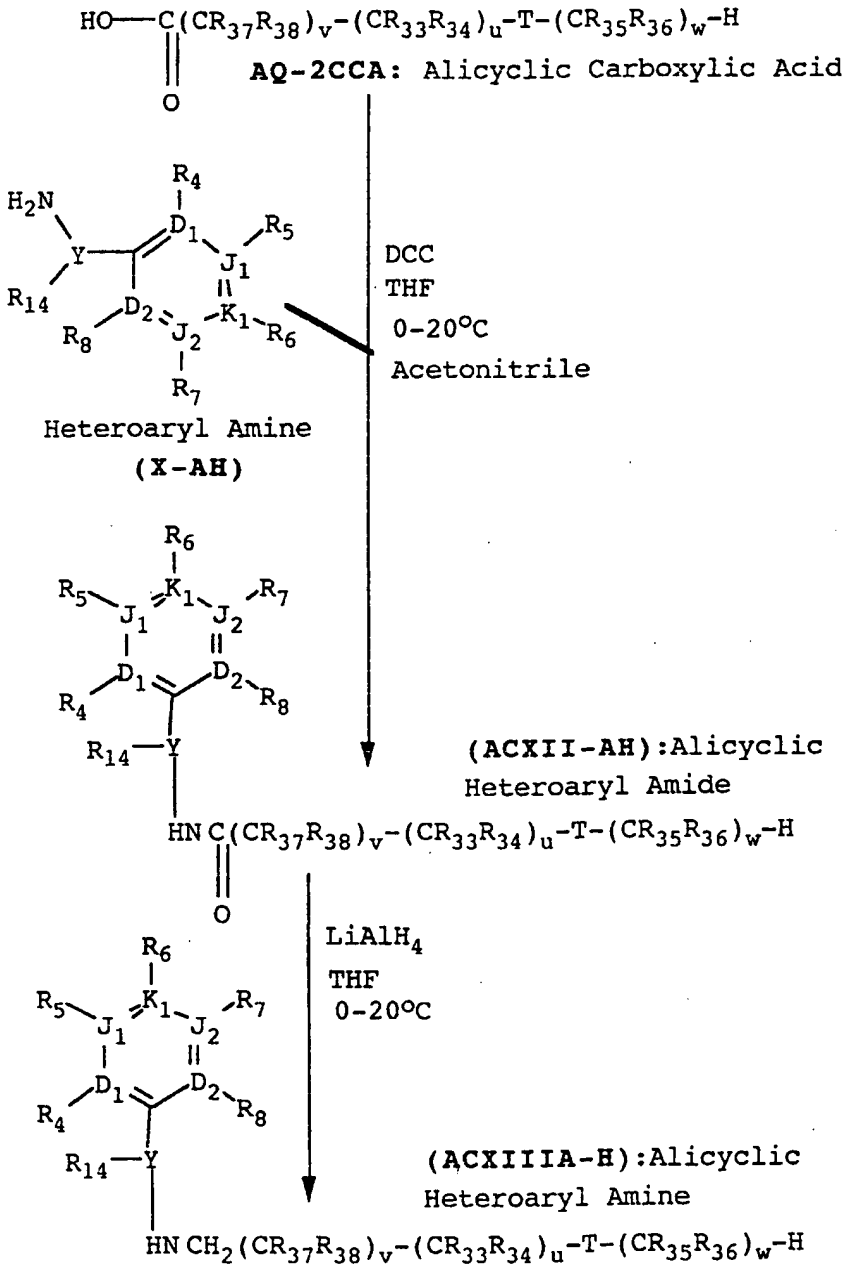
Scheme 6


AQ-2A: Cyclic Amine
TEA
Solvent
Heteroaryl Carbonyl Chloride (CCXI-AH)
(CAXII-AH): Cyclic Heteroaryl Amide
LiAlH4
THF
0-20°C
(XIIIA-H): Cyclic Heteroaryl Amine

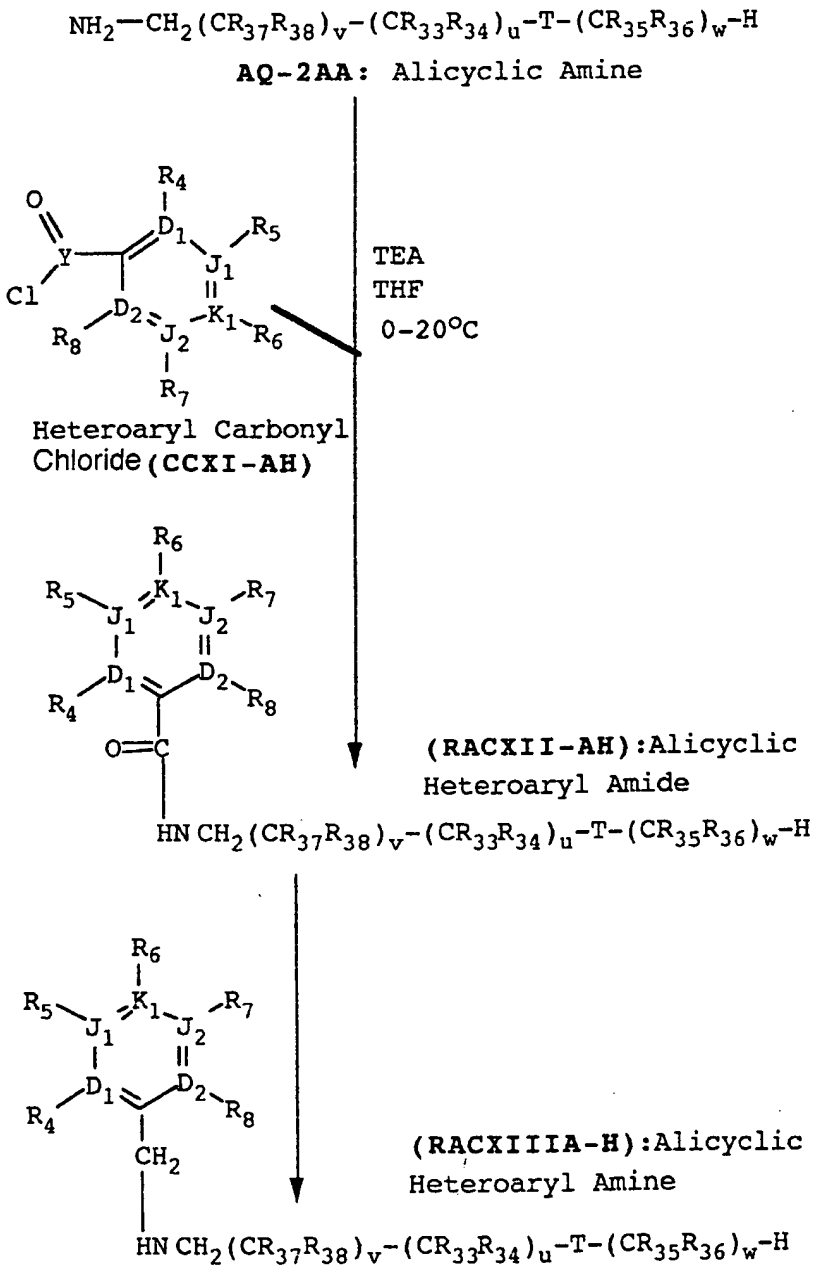
Scheme 7


NH2—CH2(CR37R38)v-(CR33R34)u-T-(CR35R36)w-H
AQ-2AA: Alicyclic Amine
TEA
THF
0-20°C
Heteroaryl Carbonyl Chloride (CCXI-AH)
(RACXII-AH):Alicyclic Heteroaryl Amide
HN CH2(CR37R38)v-(CR33R34)u-T-(CR35R36)w-H
(RACXIIIA-H):Alicyclic Heteroaryl Amine
HN CH2(CR37R38)v-(CR33R34)u-T-(CR35R36)w-H

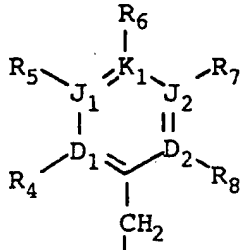
Scheme 8


HO—C(CR37R38)v-(CR33R34)u-T-(CR35R36)w-H
O
AQ-2CCA: Alicyclic Carboxylic Acid
DCC
THF
0-20°C
Acetonitrile
Heteroaryl Amine
(X-AH)
(ACXII-AH):Alicyclic
Heteroaryl Amide
HN C(CR37R38)v-(CR33R34)u-T-(CR35R36)w-H
O
LiAlH4
THF
0-20°C
(ACXIIIA-H):Alicyclic
Heteroaryl Amine
HN CH2(CR37R38)v-(CR33R34)u-T-(CR35R36)w-H

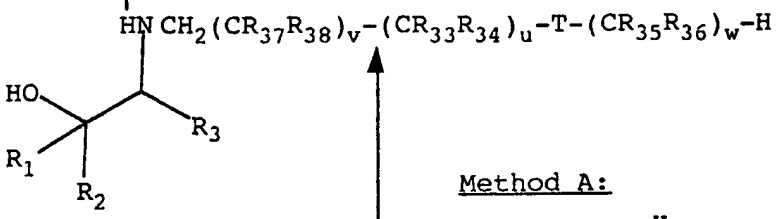
Scheme 9


NH2—CH2(CR37R38)v-(CR33R34)u-T-(CR35R36)w-H
AQ-2AA: Alicyclic Amine
TEA
THF
0-20°C
Heteroaryl Carbonyl Chloride (CCXI-AH)
(RACXII-AH):Alicyclic Heteroaryl Amide
HN CH2(CR37R38)v-(CR33R34)u-T-(CR35R36)w-H
(RACXIIIA-H):Alicyclic Heteroaryl Amine
HN CH2(CR37R38)v-(CR33R34)u-T-(CR35R36)w-H

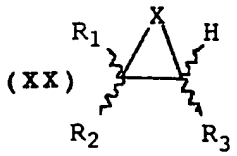
Scheme 10



(I-WO/I-WOPA/I-WOHA):Alicyclic Aryl/Heteroaryl Aminoalcoholcs



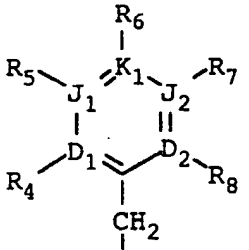
Method A:

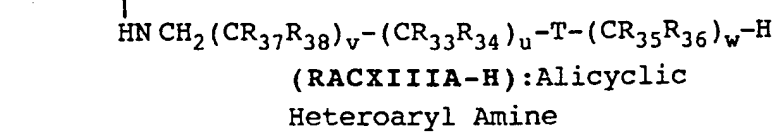


(XX)

60-90°C/THF/Lewis Acid

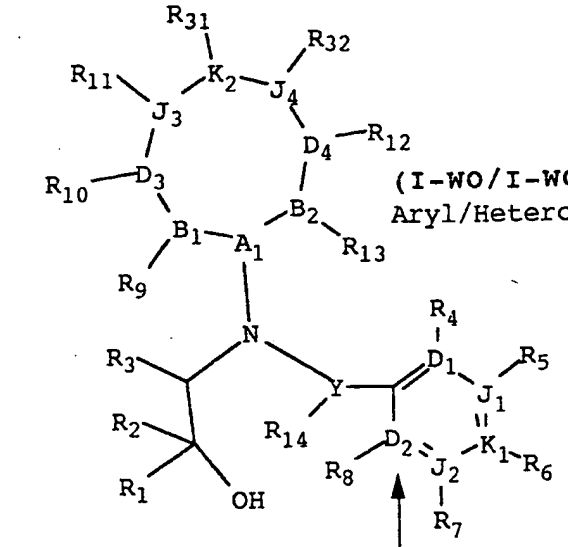
(X = O)





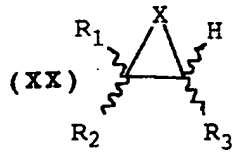
(RACXIIIA-H):Alicyclic Heteroaryl Amine

Scheme 11



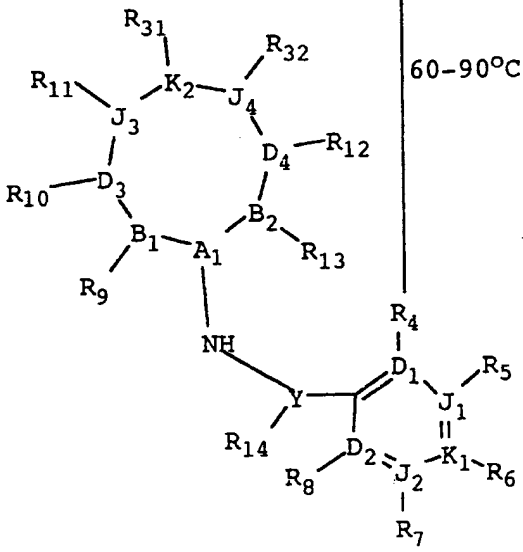
(I-WO/I-WOPC/I-WOHC):Cyclic Aryl/Heteroaryl Aminoalcoholcs

Method A:



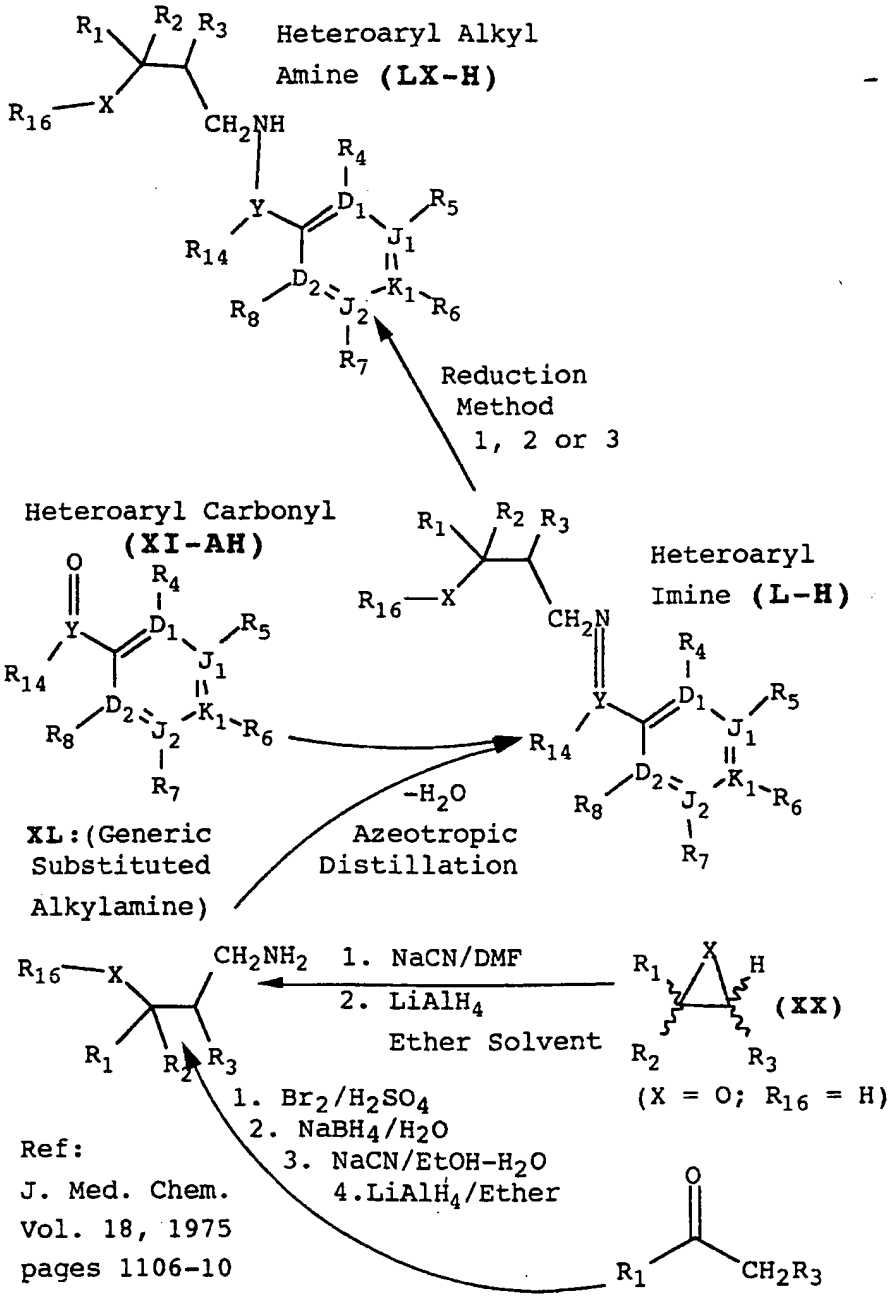
(XX)

60-90°C/THF/Lewis Acid
(X = O)

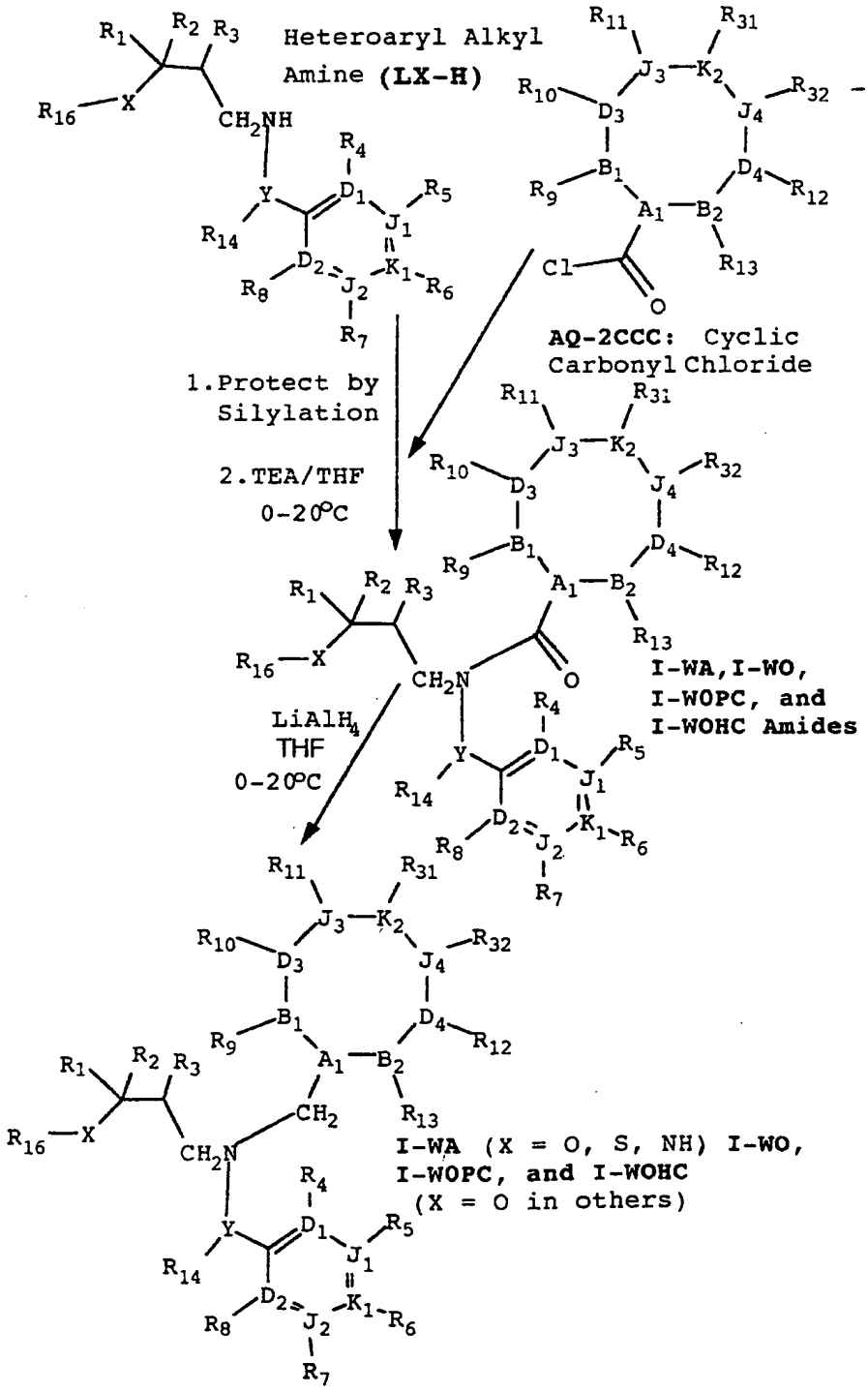


Secondary Cyclic Heteroaryl Amine (XIIIA-H)

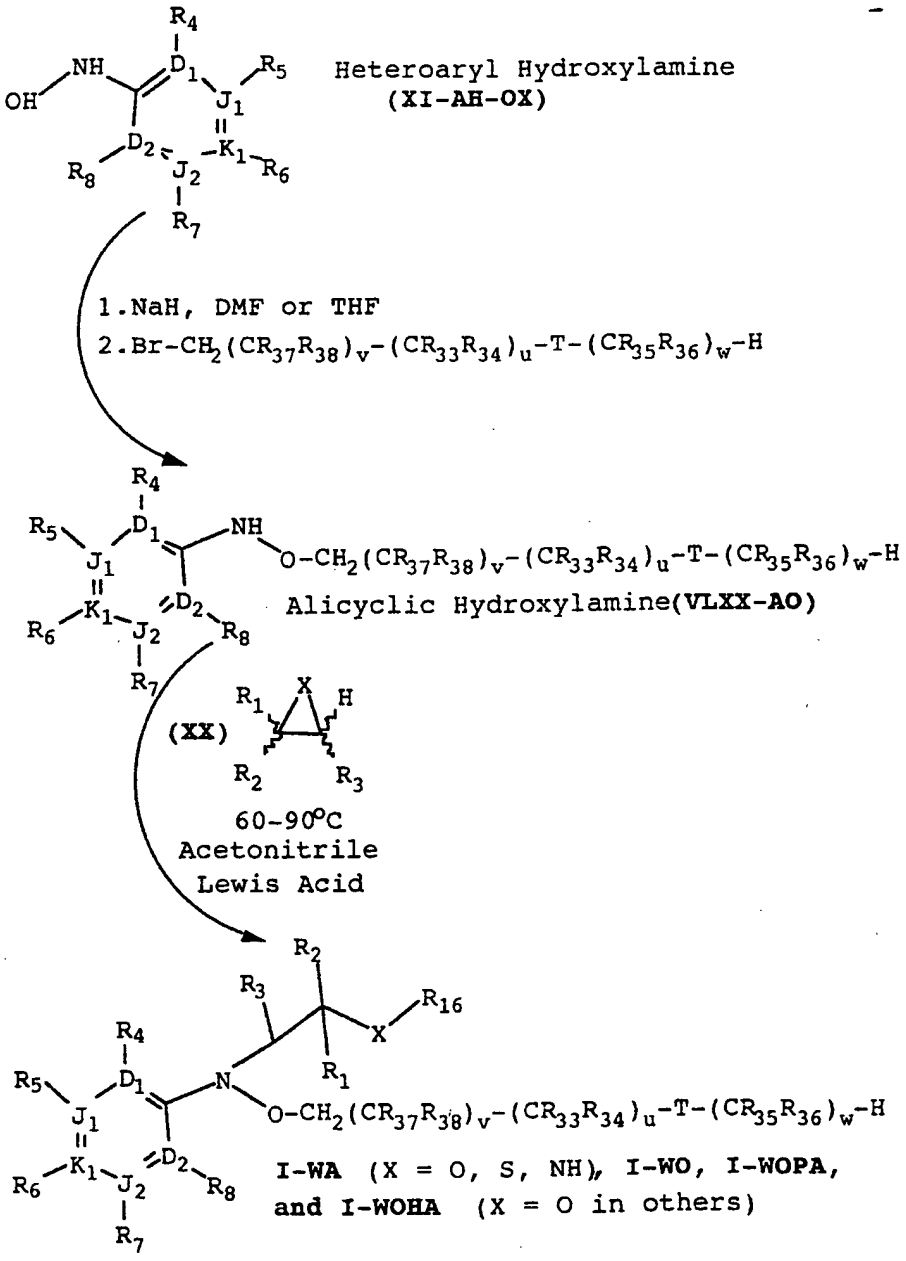
Scheme 12


Heteroaryl Alkyl Amine (LX-H)
Reduction Method 1, 2 or 3
Heteroaryl Carbonyl (XI-AH)
Heteroaryl Imine (L-H)
XL:(Generic Substituted Alkylamine)
-H2O Azeotropic Distillation
1. NaCN/DMF
2. LiAlH4
Ether Solvent
(XX)
(X = O; R16 = H)
1. Br2/H2SO4
2. NaBH4/H2O
3. NaCN/EtOH-H2O
4.LiAlH4/Ether
Ref:
J. Med. Chem.
Vol. 18, 1975
pages 1106-10

Scheme 13


Heteroaryl Alkyl Amine (LX-H)
AQ-2CCC: Cyclic Carbonyl Chloride
1.Protect by Silylation
2.TEA/THF
0-20°C
LiAlH4
THF
0-20°C
I-WA,I-WO, I-WOPC, and I-WOHC Amides
I-WA (X = O, S, NH) I-WO, I-WOPC, and I-WOHC (X = O in others)

Scheme 14

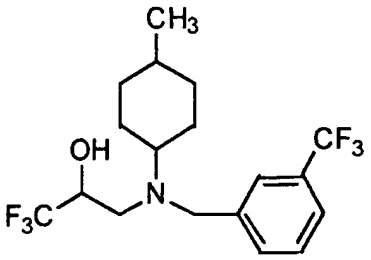

Heteroaryl Hydroxylamine
(XI-AH-OX)
1.NaH, DMF or THF
2.Br-CH2(CR37R38)v-(CR33R34)u-T-(CR35R36)w-H
O-CH2(CR37R38)v-(CR33R34)u-T-(CR35R36)w-H
Alicyclic Hydroxylamine(VLXX-AO)
(XX)
60-90°C
Acetonitrile
Lewis Acid
O-CH2(CR37R38)v-(CR33R34)u-T-(CR35R36)w-H
I-WA (X = O, S, NH), I-WO, I-WOPA,
and I-WOHA (X = O in others)

The following examples are provided to illustrate the present invention and are not intended to limit the scope thereof. Without further elaboration, it is believed that one skilled in the art can, using the preceding descriptions, utilize the present invention to its fullest extent. Therefore the following preferred specific embodiments are to be construed as merely illustrative and not limitative of the remainder of the disclosure in any way whatsoever. Compounds containing multiple variations of the structural modifications illustrated in the preceding schemes or the following Examples are also contemplated. Those skilled in the art will readily understand that known variations of the conditions and processes of the following preparative procedures can be used to prepare these compounds.

One skilled in the art may use these generic methods to prepare the following specific examples, which have been or may be properly characterized by ^{1}H NMR and mass spectrometry. These compounds also may be formed in vivo.

The following examples contain detailed descriptions of the methods of preparation of compounds of Formula V-H. These detailed descriptions fall within the scope and are presented for illustrative purposes only and are not intended as a restriction on the scope of the invention. All parts are by weight and temperatures are Degrees centigrade unless otherwise indicated.

EXAMPLE 1



3-[(4-methylcyclohexyl)[[(3-trifluoromethyl)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol

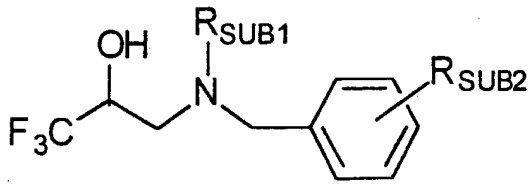
EX-1A) 4-Methylcyclohexylamine (1.15 g, 10 mmol, 97%, mixture of *cis* and *trans* isomers) and 3-trifluoromethylbenzaldehyde (1.74 g, 10 mmol) were dissolved in anhydrous chloroform (25 mL) and heated under reflux for 4 h using a Dean-Stark trap to remove water. The volatile components were removed *in vacuo* to give the desired imine (2.69 g) product quantitatively as a colorless oil, MS *m/z* = 269 [M^+]. The oil was dissolved in methanol, and after cooling to 0 °C, solid sodium borohydride was added (0.64 g, 17 mmol). The mixture was allowed to warm to room temperature and stirred for 2 h, then acidified with 1 N HCl solution. After neutralizing to pH 7.5 with 2.5 N sodium hydroxide, the mixture was extracted with diethyl ether (3 x 20 mL). The organic layer was washed with brine and water, then dried over anhydrous $MgSO_4$, and evaporated to give 1.96 g (68.4%) of the desired *N*-(4-methylcyclohexyl)[[3-(trifluoromethyl)-phenyl]methyl]amine product as a colorless oil, which was greater than 90% pure by reverse phase HPLC analysis. MS *m/z* = 271 [M^+].

EX-1B) The benzylamine product from **EX-1A** (1.08 g, 4 mmol) and 3,3,3-trifluoro-1,2-epoxypropane (0.67 g, 6 mmol) were dissolved in 1.0 mL of acetonitrile. Ytterbium (III) trifluoromethanesulfonate (0.21 g, 0.33 mmol) was added, and the stirred solution was warmed to 50 °C for 2 h under an atmosphere

of nitrogen, at which time HPLC analysis indicated that no amine starting material remained. The reaction was quenched with water and extracted with ether. The ether layer was washed with water and brine, then dried over anhydrous $MgSO_4$. The crude product was purified by flash column chromatography on silica gel eluting with ethyl acetate in hexane (1:12) to give 1.18 g (77%) of the desired 3-[(4-methyl-cyclohexyl)[[(3-trifluoromethyl)phenyl]-methyl]amino]-1,1,1-trifluoro-2-propanol product as a light amber oil, 99% pure by HPLC analysis. HRMS calculated for $C_{18}H_{23}F_6NO$: 384.1762 $[M+H]^+$, found: 384.1754. ^1H NMR ($CDCl_3$) δ 0.92 (dd, 3H), 1.17-1.81 (m, 8H), 1.93 (m, 1H), 2.48 (m, 1H), 2.80 (m, 2H), 3.76 (d, 2H), 3.79 (m, 1H), 3.94 (s, 1H), 7.45-7.60 (m, 4H). ^{19}F NMR ($CDCl_3$) δ -79.2 (d, 3F), -63.1 (s, 3F).

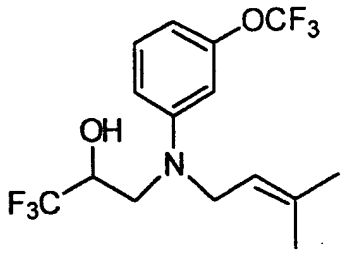
Additional substituted 3-[(*N*-alkyl and *N*-cycloalkyl)[aryl]methyl]amino-1,1,1-trifluoro-2-propanols can be prepared by one skilled in the art using similar methods, as shown in Example Table 1.

Example Table 1. Substituted 3-[(*N*-alkyl and *N*-cycloalkyl)[aryl]methyl]amino-1,1,1-trifluoro-2-propanols.



Ex. No.	R_{SUB1}	R_{SUB2}	Calculated Mass $[M+H]^+$	Observed Mass $[M+H]^+$
2	cyclopropyl	4-OCF_3	344.1085	344.1086
3	isopropyl	4-OCF_3	346.1242	346.1245
4	cyclopropyl	3-OCF_3	344.1085	344.1085
5	isopropyl	3-OCF_3	346.1242	346.1239
6	*n*-propyl	3-OCF_3	346.1242	346.1252
7	cyclopentyl	3-OCF_3	372.1398	372.1409

EXAMPLE 8



3-[(3-methyl-2-butenyl)[(3-(trifluoromethoxy)phenyl] amino]-1,1,1-trifluoro-2-propanol

EX-8A) 3-Trifluoromethoxy aniline (23.81 g, 134.4 mmol) and 3,3,3-trifluoro-1,2-epoxypropane (3.76 g, 33.6 mmol) were placed into a sealed tube

and heated at 80 °C for 24 h. The excess aniline was removed by distillation (70 °C at 80 torr). The resulting residue contained 8.6 g (>95%) of the desired 3-[[(trifluoromethoxy)phenyl]-amino]-1,1,1-trifluoro-2-propanol product as a light yellow oil. ^{1}H NMR ($CDCl_3$) δ 3.29-3.37 (m, 1H), 3.55 (dd, 1H), 4.20 (m, 1H), 6.48-6.63 (m, 3H), 7.12 (t, 1H). ^{19}F NMR ($CDCl_3$) δ -79.36 (s, 3F), -58.44 (s, 3F).

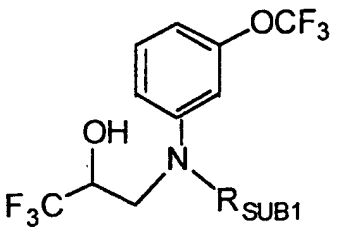
EX-8B) The 3-[[(trifluoromethoxy)phenyl]amino]-1,1,1-trifluoro-2-propanol product from **EX-8A** (18.68 g, 64.6 mmol) and imidazole (10.99 g, 0.162 mmol) were dissolved in dimethylformamide (40.0 mL) and *t*-butyldimethylsilylchloride (11.69 g, 77.6 mmol) was added in 3.0 g portions over 15 min. The reaction was stirred at 23 °C for 18 h. The resulting solution was diluted with ethyl acetate and washed with water and brine. The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel eluting with 25% ethyl acetate in hexane to afford 17.08g of the desired silylated product as a light golden oil. FABMS *m/z* = 404 $[M+H]^+$. ^{1}H NMR ($CDCl_3$) δ 0.042 (s, 3H), 0.085 (s, 3H), 0.91 (s, 9H), 3.25-3.35 (m, 1H), 3.50 (dd, 1H), 4.10 (m, 1H), 6.40 (bs, 1H), 6.50 (dd, 1H), 6.59 (d, 1H), 7.17 (t, 1H).

EX-8C) The silylated product from **EX-8B** (0.15 g, 0.372 mmol) was dissolved in THF (0.5 mL) in a 2-dram glass vial with stir bar and cooled to 0 °C in an ice bath. KO*t*Bu (1 M in THF, 1.2 eq, 0.446 mmol, 0.446 mL) was added to the cold solution in one portion. The reaction mixture was stirred at 0 °C for 5 min, then 1-chloro-3-methyl-2-butene (38.9 mg, 0.372 mmol) in 0.5 mL of THF was added in one portion to the cold reaction mixture. The ice bath was removed, and the reaction was stirred at 23 °C for 18 h. The resulting solution was diluted with ethyl acetate and washed with water and brine. The organic layer was dried

($MgSO_4$) and concentrated under a nitrogen stream. The crude residue was dissolved in 2.0 mL of THF and treated with tetrabutylammonium fluoride (1 M in THF, 1.2 eq, 0.446 mmol, 0.446 mL). The reaction mixture was stirred at 23 °C for 3 h. The reaction was diluted with ethyl acetate and washed with water and brine. The organic layer wad dried ($MgSO_4$) and concentrated under a nitrogen stream. The crude residue was purified using 0.5 g of silica gel eluting with hexane (100%) followed by 30% ethyl acetate in hexane to give 59.1 mg (44.4% yield) of the desired 3-[(3-methyl-2-butenyl)[(3-(trifluoromethoxy)-phenyl]amino]- 1,1,1-trifluoro-2-propanol product as a golden oil. FABMS *m/z* = 358 $[M+H]^+$.

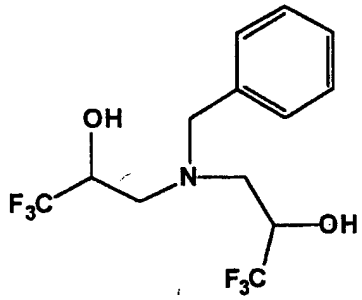
Additional examples of substituted 3-[(*N*-alkyl, *N*-alkenyl and *N*-alkynyl)-[(trifluoromethoxy)phenyl] amino]-1,1,1-trifluoro-2-propanols can be prepared by one skilled in the art using similar methods, as shown in Example Table 2.

Example Table 2. 3-[(*N*-alkyl, *N*-alkenyl and *N*-alkynyl)[(trifluoromethoxy)phenyl] amino]-1,1,1-trifluoro-2-propanols.



Ex. No.	R_{SUB1}	Calculated Mol. Wt.	Observed Mass $[M+H]^+$
9	2,3-octenyl	399	400
10	2,3-propynyl	327	328
11	3-methyl-butyl	359	360
12	2-(carbomethoxy)-2-propenyl	387	388
13	3-(carbomethoxy)-2-propenyl	387	388
14	4-methoxy-2-butenyl	373	374

EXAMPLE 15



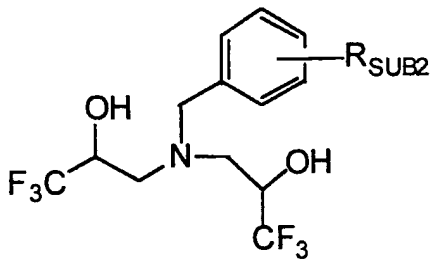
1,1'-[(Phenylmethyl)imino]bis[3,3,3-trifluoro-2-propanol]

Benzylamine (1.5 eq, 2.88 g, 2.94 mL, 26.8 mmol) was combined with 3,3,3-trifluoro-1,2-epoxypropane (2.0 g, 17.86 mmol) in a sealed glass tube and

heated at 80 °C for 18 h. Upon cooling to room temperature, the reaction mixture formed a slushy white solid. The solid was collected by filtration and washed with diethyl ether. The mother liquor was concentrated *in vacuo* to give 1.71 g (43%) of the desired 1,1'-[(phenyl-methyl)imino]bis[3,3,3-trifluoro-2-propanol] product as a colorless oil. FABMS *m/z* = 332 $[M+H]^+$. ^1H NMR ($CDCl_3$) δ 2.85-2.96 (m, 4H) , 3.94 (s, 2H), 3.94-3.97 (m, 2H), 7.24- 7.37 (m, 5H).

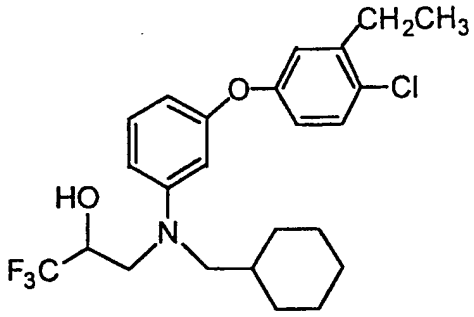
Additional examples of substituted 1,1'-[(phenylmethyl)imino]bis[3,3,3-tri-fluoro-2-propanols] can be prepared by one skilled in the art using similar methods, as shown in Example Table 3.

Example Table 3. Substituted 1,1'-[(phenylmethyl)imino]bis[3,3,3-trifluoro-2-propanols]



Ex. No.	R_{SUB2}	Calculated Mass $[M+H]^+$	Observed Mass $[M+H]^+$
16	3-trifluoromethyl	400.0959	400.0923
17	4-trifluoromethoxy	416.0908	416.0905

EXAMPLE 18



3-[[3-(4-chloro-3-ethylphenoxy)phenyl][3-cyclohexylmethyl]amino]-1,1,1-trifluoro-2-propanol

EX-18A) To a solution of 1,3-dinitrobenzene (16.8 g, 0.1 mol) and 4-chloro-3-ethylphenol (15.6 g, 0.1 mol) in 200 mL of dimethylsulfoxide was added cesium carbonate (65 g, 0.2 mol). The reaction mixture was heated at 100 °C under nitrogen overnight then cooled to room temperature. The reaction mixture was filtered through celite then rinsed with diethyl ether and a small amount of water. The filtrate was extracted several times with diethyl ether. The organic layers were combined, washed with water and brine, dried over $MgSO_4$, and concentrated *in vacuo* to give 21.8 g (78%) of the desired 3-(4-chloro-3-ethylphenoxy)-1-nitrobenzene product as a dark orange oil, which was greater than 90% pure by reverse phase HPLC analysis. HRMS calcd. for $C_{14}H_{12}ClNO_3$: 295.0849 $[M+NH_4]^+$, found 295.0862.

EX-18B) To a solution of 3-(4-chloro-3-ethylphenoxy)-1-nitrobenzene (10 g, 0.036 mol) from **EX-18A** in 400 mL of glacial acetic acid and 1 mL of water was added zinc metal (20 g, 0.305 mol) at room temperature, and the resultant mixture was stirred for 1 h. The reaction mixture was filtered through celite. The filtrate was neutralized with ammonium hydroxide and extracted with diethyl ether. The organic layer was washed with water and brine, dried over $MgSO_4$,

and concentrated *in vacuo* to give 10 g (100%) of the desired 3-(4-chloro-3-ethylphenoxy)aniline product as a dark orange oil, which was greater than 90% pure by reverse phase HPLC analysis. HRMS calcd. for $C_{14}H_{14}ClNO$: 248.0842 $[M+H]^+$, found: 248.0833.

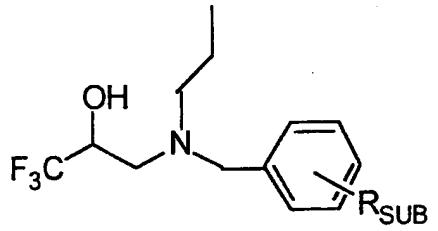
EX-18C) The 3-(4-chloro-3-ethylphenoxy)aniline (0.545 g, 0.002 mol) product from **EX-18B** was mixed with neat 3,3,3-trifluoro-1,2-epoxypropane (0.220 g, 0.002 mol) in a pressurized vial. The resulting mixture was heated at 90 °C for 18 h, cooled, and the excess 3,3,3-trifluoro-1,2-epoxypropane was removed *in vacuo*. The crude product was purified by flash column chromatography on silica gel eluting with 1:4 ethyl acetate in hexane to give 0.254 g (35%) of the desired 3-[[3-(4-chloro-3-ethyl-phenoxy)phenyl]amino]-1,1,1-trifluoro-2-propanol product as a pure orange oil. Anal calcd. for $C_{17}H_{17}NOF_3Cl$: C, 56.75; H, 4.76; N, 3.89. Found: C, 56.72; H, 4.70; N, 3.85. HRMS calcd.: 360.0978 $[M+H]^+$, found: 360.0969. ^1H NMR ($CDCl_3$) δ 1.50 (t, 3H), 2.72 (m, 2H), 3.36 (m, 1H), 3.54 (m, 1H), 4.20 (m, 1H), 6.42 (m, 2H), 6.81 (dd, 1H), 6.94 (d, 1H), 7.18 (d, 1H), 7.25 (m, 2H).

The 3-[[3-(4-chloro-3-ethylphenoxy)phenyl]amino]-1,1,1-trifluoro-2-propanol product from **EX-18C** was dissolved in 12 mL of tetrahydrofuran. To this stirred solution was added cyclohexanecarboxaldehyde (0.032 g, 0.285 mmol), followed by sodium tri-acetoxyborohydride (0.079 g, 0.370 mmol and concentrated acetic acid (0.020 g, 0.325 mmol). The resulting mixture was stirred at room temperature for 18 h. Additional cyclohexanecarboxaldehyde (0.032 g, 0.285 mmol) was added and the mixture was allowed to stir at room temperature for another 18 h. The reaction was quenched with saturated sodium bicarbonate and extracted with methylene chloride. The organic layers were combined, dried over $MgSO_4$ and concentrated to an orange/brown oil. The crude product was

purified by flash column chromatography on silica gel eluting with 1:4 ethyl acetate in hexane to give 0.080 g (61%) of the desired 3-[[3-(4-chloro-3-ethylphenoxy)phenyl][3-cyclohexylmethyl]amino]-1,1,1-trifluoro-2-propanol product as a yellow-orange oil (>95% pure by HPLC). HRMS calcd.: 456.1917 $[M+H]^+$, found: 456.1942. ^1H NMR ($CDCl_3$) δ 0.82-1.01 (m, 2H), 1.22-1.27 (m, 3H), 1.73-1.76 (m, 5H), 2.74 (dd, 2H), 3.15 (dd, 2H), 3.23 (dd, 1H), 3.52 (m, 1H), 3.80 (dd, 1H), 4.28 (m, 1H), 6.34 (d, 2H), 6.42 (d, 1H), 6.83 (dd, 1H), 6.98 (d, 1H), 7.19 (t, 1H), 7.29 (d, 1H). ^{19}F NMR ($CDCl_3$) δ -79.06 (d, 3F).

Based on the preceding procedures, additional substituted 3-[(*N*-alkyl)-[[aryl]methyl]amino]-1,1,1-trifluoro-2-propanols and 3-[(*N*-cycloalkyl)-[[aryl]methyl]-amino]-halo-2-propanols are prepared by one skilled in the art using similar methods, as shown in Example Tables 4 and 5. Similarly, substituted 3-[(*N*-aryl)[[cycloalkyl]-methyl]amino]-halo-2-propanols and substituted 3-[(*N*-aryl)[[haloalkyl]methyl]amino]-halo-2-propanols are prepared by one skilled in the art using analogous methods, as shown in Example Tables 6 and 7.

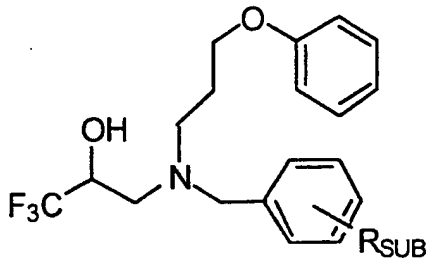
Example Table 4. 3-[(*N*-alkyl)[[aryl]methyl]amino]-1,1,1-trifluoro-2-propanols.



Ex. No.	R_{SUB}
19	4-OCF_3
20	3-OCF_2CF_2H
21	2-F, 5-CF_3
22	2-F, 4-CF_3
23	3-CF_3, 4-F
24	3-CF_3CF_2
25	3-cyclopentyl
26	3-isopropoxy
27	3-SCF_3
28	3-*sec*-butoxy
29	3-$C(CF_3)_2OH$
30	3-(2-furyl)
31	3-(3-furyl)
32	3-isobutyl
33	3-isobutoxy
34	3-ethoxy
35	3-OCH_2CF_3
36	3-propoxy
37	3-*tert*-butoxy

Ex. No.	R_{SUB}
38	3-(2-thienyl)
39	3-cyclopropyl
40	4-F, 3-(2-furyl)
41	3-(3-CF_3-phenoxy)
42	3,4-(OCF_2CF_2O)
43	3-OCF_2CF_3
44	3-cyclopentoxy
45	3-(cyclopropyl)methoxy
46	3-$OCH_2CH(OH)CF_3$
47	3-CF_3
48	4-CF_3
49	3-$CH_2CF_2CF_3$
50	3-CH_2CF_3
51	3-$CH(CF_3)_2$
52	3-$CF_2CF_2CF_3$
53	3-phenoxy
54	3-phenyl
55	3-(tetrahydro-2-furyl)
56	isoamyl

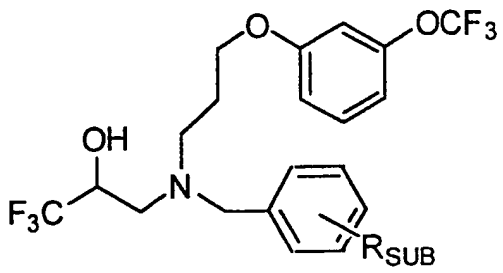
Example Table 4. (cont.) 3-[(*N*-alkyl)[[aryl]methyl]amino]-1,1,1-trifluoro-2-propanols.



Ex. No.	R_{SUB}
57	3-OCF_3
58	3-OCF_2CF_2H
59	2-F, 5-CF_3
60	2-F, 4-CF_3
61	3-CF_3, 4-F
62	3-CF_3CF_2
63	3-cyclopentyl
64	3-isopropoxy
65	3-SCF_3
66	3-*sec*-butoxy
67	3-$C(CF_3)_2OH$
68	3-(2-furyl)
69	3-(3-furyl)
70	3-isobutyl
71	3-isobutoxy
72	3-ethoxy
73	3-OCH_2CF_3
74	3-propoxy
75	3-*tert*-butoxy

Ex. No.	R_{SUB}
76	3-(2-thienyl)
77	3-cyclopropyl
78	4-F, 3-(2-furyl)
79	3-(3-CF_3-phenoxy)
80	3,4-(OCF_2CF_2O)
81	3-OCF_2CF_3
82	3-cyclopentoxy
83	3-(cyclopropyl)methoxy
84	3-$OCH_2CH(OH)CF_3$
85	3-CF_3
86	4-CF_3
87	3-$CH_2CF_2CF_3$
88	3-CH_2CF_3
89	3-$CH(CF_3)_2$
90	3-$CF_2CF_2CF_3$
91	3-phenoxy
92	3-phenyl
93	3-(tetrahydro-2-furyl)
94	isoamyl

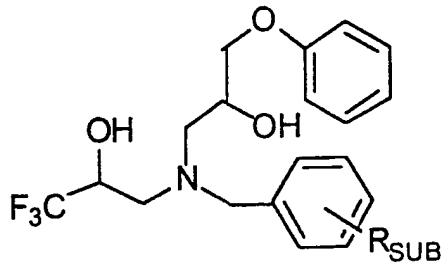
Example Table 4. (cont.) 3-[(*N*-alkyl)[[aryl]96methyl]amino]-1,1,1-trifluoro-2-propanols.



Ex. No.	R_{SUB}
95	3-OCF_3
96	3-OCF_2CF_2H
97	2-F, 5-CF_3
98	2-F, 4-CF_3
99	3-CF_3, 4-F
100	3-CF_3CF_2
101	3-cyclopentyl
102	3-isopropoxy
103	3-SCF_3
104	3-*sec*-butoxy
105	3-$C(CF_3)_2OH$
106	3-(2-furyl)
107	3-(3-furyl)
108	3-isobutyl
109	3-isobutoxy
110	3-ethoxy
111	3-OCH_2CF_3
112	3-propoxy
113	3-*tert*-butoxy

Ex. No.	R_{SUB}
114	3-(2-thienyl)
115	3-cyclopropyl
116	4-F, 3-(2-furyl)
117	3-(3-CF_3-phenoxy)
118	3,4-(OCF_2CF_2O)
119	3-OCF_2CF_3
120	3-cyclopentoxy
121	3-(cyclopropyl)methoxy
122	3-$OCH_2CH(OH)CF_3$
123	3-CF_3
124	4-CF_3
125	3-$CH_2CF_2CF_3$
126	3-CH_2CF_3
127	3-$CH(CF_3)_2$
128	3-$CF_2CF_2CF_3$
129	3-phenoxy
130	3-phenyl
131	3-(tetrahydro-2-furyl)
132	isoamyl

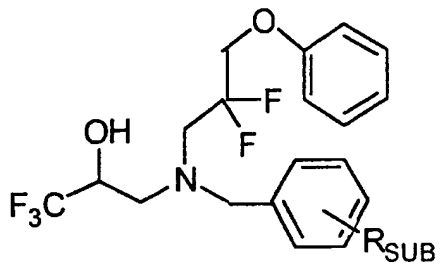
Example Table 4. (cont.) 3-[(*N*-alkyl)[[aryl]methyl]amino]-1,1,1-trifluoro-2-propanols.



Ex. No.	R_{SUB}
133	3-OCF_3
134	3-OCF_2CF_2H
135	2-F, 5-CF_3
136	2-F, 4-CF_3
137	3-CF_3, 4-F
138	3-CF_3CF_2
139	3-cyclopentyl
140	3-isopropoxy
141	3-SCF_3
142	3-*sec*-butoxy
143	3-$C(CF_3)_2OH$
144	3-(2-furyl)
145	3-(3-furyl)
146	3-isobutyl
147	3-isobutoxy
148	3-ethoxy
149	3-OCH_2CF_3
150	3-propoxy
151	3-*tert*-butoxy

Ex. No.	R_{SUB}
152	3-(2-thienyl)
153	3-cyclopropyl
154	4-F, 3-(2-furyl)
155	3-(3-CF_3-phenoxy)
156	3,4-(OCF_2CF_2O)
157	3-OCF_2CF_3
158	3-cyclopentoxy
159	3-(cyclopropyl)methoxy
160	3-$OCH_2CH(OH)CF_3$
161	3-CF_3
162	4-CF_3
163	3-$CH_2CF_2CF_3$
164	3-CH_2CF_3
165	3-$CH(CF_3)_2$
166	3-$CF_2CF_2CF_3$
167	3-phenoxy
168	3-phenyl
169	3-(tetrahydro-2-furyl)
170	isoamyl

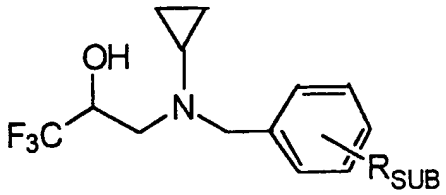
Example Table 4. (cont.) 3-[(*N*-alkyl)[[aryl]methyl]amino]-1,1,1-trifluoro-2-propanols.



Ex. No.	R_{SUB}
171	3-OCF_3
172	3-OCF_2CF_2H
173	2-F, 5-CF_3
174	2-F, 4-CF_3
175	3-CF_3, 4-F
176	3-CF_3CF_2
177	3-cyclopentyl
178	3-isopropoxy
179	3-SCF_3
180	3-*sec*-butoxy
181	3-$C(CF_3)_2OH$
182	3-(2-furyl)
183	3-(3-furyl)
184	3-isobutyl
185	3-isobutoxy
186	3-ethoxy
187	3-OCH_2CF_3
188	3-propoxy
189	3-*tert*-butoxy

Ex. No.	R_{SUB}
190	3-(2-thienyl)
191	3-cyclopropyl
192	4-F, 3-(2-furyl)
193	3-(3-CF_3-phenoxy)
194	3,4-(OCF_2CF_2O)
195	3-OCF_2CF_3
196	3-cyclopentoxy
197	3-(cyclopropyl)methoxy
198	3-$OCH_2CH(OH)CF_3$
199	3-CF_3
200	4-CF_3
201	3-$CH_2CF_2CF_3$
202	3-CH_2CF_3
203	3-$CH(CF_3)_2$
204	3-$CF_2CF_2CF_3$
205	3-phenoxy
206	3-phenyl
207	3-(tetrahydro-2-furyl)
208	isoamyl

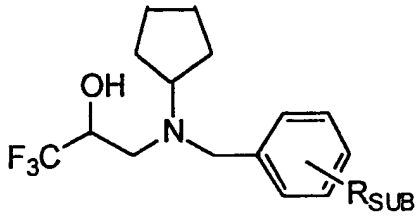
Example Table 5. 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-1,1,1-trifluoro-2-propanols.



Ex. No.	R_{SUB}
209	3-*tert*-butoxy
210	3-OCF_2CF_2H
211	2-F, 5-CF_3
212	2-F, 4-CF_3
213	3-CF_3, 4-F
214	3-CF_3CF_2
215	3-cyclopentyl
216	3-isopropoxy
217	3-SCF_3
218	3-*sec*-butoxy
219	3-$C(CF_3)_2OH$
220	3-(2-furyl)
221	3-(3-furyl)
222	3-isobutyl
223	3-isobutoxy
224	3-ethoxy
225	3-OCH_2CF_3
226	3-propoxy
227	3-(2-pyridyl)

Ex. No.	R_{SUB}
228	3-(2-thienyl)
229	3-cyclopropyl
230	4-F, 3-(2-furyl)
231	3-(3-CF_3-phenoxy)
232	3,4-(OCF_2CF_2O)
233	3-OCF_2CF_3
234	3-cyclopentoxy
235	3-(cyclopropyl)methoxy
236	3-$OCH_2CH(OH)CF_3$
237	3-CF_3
238	4-CF_3
239	3-$CH_2CF_2CF_3$
240	3-CH_2CF_3
241	3-$CH(CF_3)_2$
242	3-$CF_2CF_2CF_3$
243	3-phenoxy
244	3-phenyl
245	3-(tetrahydro-2-furyl)
246	isoamyl

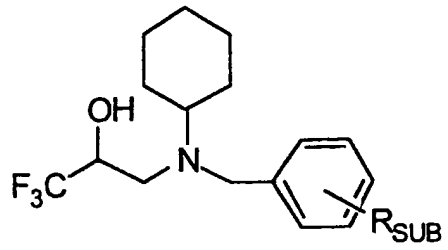
Example Table 5. (cont.). 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB}
247	4-OCF_3
248	3-OCF_2CF_2H
249	2-F, 5-CF_3
250	2-F, 4-CF_3
251	3-CF_3, 4-F
252	3-CF_3CF_2
253	3-cyclopentyl
254	3-isopropoxy
255	3-SCF_3
256	3-*sec*-butoxy
257	3-$C(CF_3)_2OH$
258	3-(2-furyl)
259	3-(3-furyl)
260	3-isobutyl
261	3-isobutoxy
262	3-ethoxy
263	3-OCH_2CF_3
264	3-propoxy
265	3-*tert*-butoxy

Ex. No.	R_{SUB}
266	3-(2-thienyl)
267	3-cyclopropyl
268	4-F, 3-(2-furyl)
269	3-(3-CF_3-phenoxy)
270	3,4-(OCF_2CF_2O)
271	3-OCF_2CF_3
272	3-cyclopentoxy
273	3-(cyclopropyl)methoxy
274	3-$OCH_2CH(OH)CF_3$
275	3-CF_3
276	4-CF_3
277	3-$CH_2CF_2CF_3$
278	3-CH_2CF_3
279	3-$CH(CF_3)_2$
280	3-$CF_2CF_2CF_3$
281	3-phenoxy
282	3-phenyl
283	3-(tetrahydro-2-furyl)
284	isoamyl

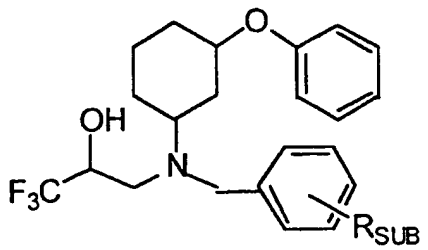
Example Table 5. (cont.). 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB}
285	3-OCF_3
286	3-OCF_2CF_2H
287	2-F, 5-CF_3
288	2-F, 4-CF_3
289	3-CF_3, 4-F
290	3-CF_3CF_2
291	3-cyclopentyl
292	3-isopropoxy
293	3-SCF_3
294	3-*sec*-butoxy
295	3-$C(CF_3)_2OH$
296	3-(2-furyl)
297	3-(3-furyl)
298	3-isobutyl
299	3-isobutoxy
300	3-ethoxy
301	3-OCH_2CF_3
302	3-propoxy
303	3-*tert*-butoxy

Ex. No.	R_{SUB}
304	3-(2-thienyl)
305	3-cyclopropyl
306	4-F, 3-(2-furyl)
307	3-(3-CF_3-phenoxy)
308	3,4-(OCF_2CF_2O)
309	3-OCF_2CF_3
310	3-cyclopentoxy
311	3-(cyclopropyl)methoxy
312	3-$OCH_2CH(OH)CF_3$
313	3-CF_3
314	4-CF_3
315	3-$CH_2CF_2CF_3$
316	3-CH_2CF_3
317	3-$CH(CF_3)_2$
318	3-$CF_2CF_2CF_3$
319	3-phenoxy
320	3-phenyl
321	3-(tetrahydro-2-furyl)
322	isoamyl

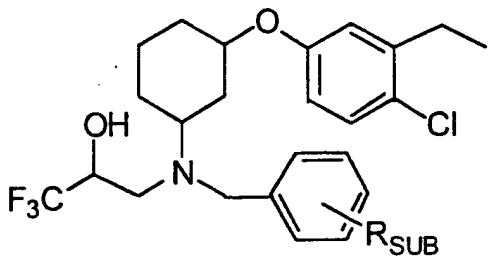
Example Table 5. (cont.). 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB}
323	3-OCF_3
324	3-OCF_2CF_2H
325	2-F, 5-CF_3
326	2-F, 4-CF_3
327	3-CF_3, 4-F
328	3-CF_3CF_2
329	3-cyclopentyl
330	3-isopropoxy
331	3-SCF_3
332	3-*sec*-butoxy
333	3-$C(CF_3)_2OH$
334	3-(2-furyl)
335	3-(3-furyl)
336	3-isobutyl
337	3-isobutoxy
338	3-ethoxy
339	3-OCH_2CF_3
340	3-propoxy
341	3-*tert*-butoxy

Ex. No.	R_{SUB}
342	3-(2-thienyl)
343	3-cyclopropyl
344	4-F, 3-(2-furyl)
345	3-(3-CF_3-phenoxy)
346	3,4-(OCF_2CF_2O)
347	3-OCF_2CF_3
348	3-cyclopentoxy
349	3-(cyclopropyl)methoxy
350	3-$OCH_2CH(OH)CF_3$
351	3-CF_3
352	4-CF_3
353	3-$CH_2CF_2CF_3$
354	3-CH_2CF_3
355	3-$CH(CF_3)_2$
356	3-$CF_2CF_2CF_3$
357	3-phenoxy
358	3-phenyl
359	3-(tetrahydro-2-furyl)
360	isoamyl

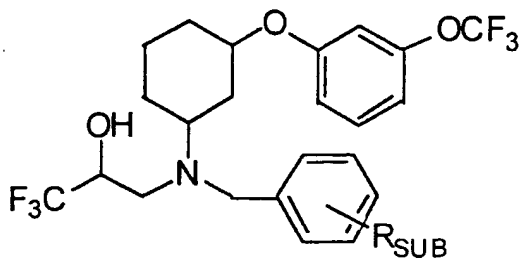
Example Table 5. (cont.). 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB}
361	3-OCF_3
362	3-OCF_2CF_2H
363	2-F, 5-CF_3
364	2-F, 4-CF_3
365	3-CF_3, 4-F
366	3-CF_3CF_2
367	3-cyclopentyl
368	3-isopropoxy
369	3-SCF_3
370	3-*sec*-butoxy
371	3-$C(CF_3)_2OH$
372	3-(2-furyl)
373	3-(3-furyl)
374	3-isobutyl
375	3-isobutoxy
376	3-ethoxy
377	3-OCH_2CF_3
378	3-propoxy
379	3-*tert*-butoxy

Ex. No.	R_{SUB}
380	3-(2-thienyl)
381	3-cyclopropyl
382	4-F, 3-(2-furyl)
383	3-(3-CF_3-phenoxy)
384	3,4-(OCF_2CF_2O)
385	3-OCF_2CF_3
386	3-cyclopentoxy
387	3-(cyclopropyl)methoxy
388	3-$OCH_2CH(OH)CF_3$
389	3-CF_3
390	4-CF_3
391	3-$CH_2CF_2CF_3$
392	3-CH_2CF_3
393	3-$CH(CF_3)_2$
394	3-$CF_2CF_2CF_3$
395	3-phenoxy
396	3-phenyl
397	3-(tetrahydro-2-furyl)
398	isoamyl

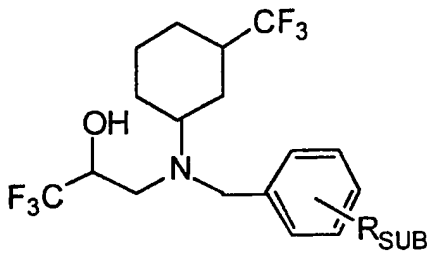
Example Table 5. (cont.). 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB}
399	3-OCF_3
400	3-OCF_2CF_2H
401	2-F, 5-CF_3
402	2-F, 4-CF_3
403	3-CF_3, 4-F
404	3-CF_3CF_2
405	3-cyclopentyl
406	3-isopropoxy
407	3-SCF_3
408	3-*sec*-butoxy
409	3-$C(CF_3)_2OH$
410	3-(2-furyl)
411	3-(3-furyl)
412	3-isobutyl
413	3-isobutoxy
414	3-ethoxy
415	3-OCH_2CF_3
416	3-propoxy
417	3-*tert*-butoxy

Ex. No.	R_{SUB}
418	3-(2-thienyl)
419	3-cyclopropyl
420	4-F, 3-(2-furyl)
421	3-(3-CF_3-phenoxy)
422	3,4-(OCF_2CF_2O)
423	3-OCF_2CF_3
424	3-cyclopentoxy
425	3-(cyclopropyl)methoxy
426	3-$OCH_2CH(OH)CF_3$
427	3-CF_3
428	4-CF_3
429	3-$CH_2CF_2CF_3$
430	3-CH_2CF_3
431	3-$CH(CF_3)_2$
432	3-$CF_2CF_2CF_3$
433	3-phenoxy
434	3-phenyl
435	3-(tetrahydro-2-furyl)
436	isoamyl

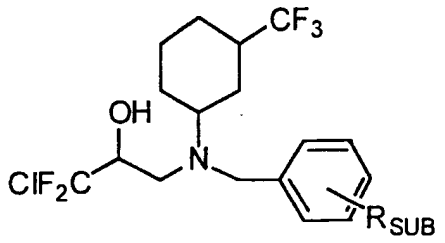
Example Table 5. (cont.). 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB}
437	3-OCF_3
438	3-OCF_2CF_2H
439	2-F, 5-CF_3
440	2-F, 4-CF_3
441	3-CF_3, 4-F
442	3-CF_3CF_2
443	3-cyclopentyl
444	3-isopropoxy
445	3-SCF_3
446	3-*sec*-butoxy
447	3-$C(CF_3)_2OH$
448	3-(2-furyl)
449	3-(3-furyl)
450	3-isobutyl
451	3-isobutoxy
452	3-ethoxy
453	3-OCH_2CF_3
454	3-propoxy
455	3-*tert*-butoxy

Ex. No.	R_{SUB}
456	3-(2-thienyl)
457	3-cyclopropyl
458	4-F, 3-(2-furyl)
459	3-(3-CF_3-phenoxy)
460	3,4-(OCF_2CF_2O)
461	3-OCF_2CF_3
462	3-cyclopentoxy
463	3-(cyclopropyl)methoxy
464	3-$OCH_2CH(OH)CF_3$
465	3-CF_3
466	4-CF_3
467	3-$CH_2CF_2CF_3$
468	3-CH_2CF_3
469	3-$CH(CF_3)_2$
470	3-$CF_2CF_2CF_3$
471	3-phenoxy
472	3-phenyl
473	3-(tetrahydro-2-furyl)
474	isoamyl

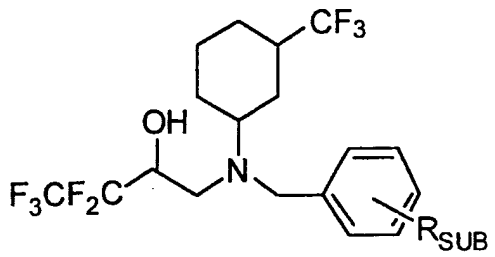
Example Table 5. (cont.). 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB}
475	3-OCF_3
476	3-OCF_2CF_2H
477	2-F, 5-CF_3
478	2-F, 4-CF_3
479	3-CF_3, 4-F
480	3-CF_3CF_2
481	3-cyclopentyl
482	3-isopropoxy
483	3-SCF_3
484	3-*sec*-butoxy
485	3-$C(CF_3)_2OH$
486	3-(2-furyl)
487	3-(3-furyl)
488	3-isobutyl
489	3-isobutoxy
490	3-ethoxy
491	3-OCH_2CF_3
492	3-propoxy
493	3-*tert*-butoxy

Ex. No.	R_{SUB}
494	3-(2-thienyl)
495	3-cyclopropyl
496	4-F, 3-(2-furyl)
497	3-(3-CF_3-phenoxy)
498	3,4-(OCF_2CF_2O)
499	3-OCF_2CF_3
500	3-cyclopentoxy
501	3-(cyclopropyl)methoxy
502	3-$OCH_2CH(OH)CF_3$
503	3-CF_3
504	4-CF_3
505	3-$CH_2CF_2CF_3$
506	3-CH_2CF_3
507	3-$CH(CF_3)_2$
508	3-$CF_2CF_2CF_3$
509	3-phenoxy
510	3-phenyl
511	3-(tetrahydro-2-furyl)
512	isoamyl

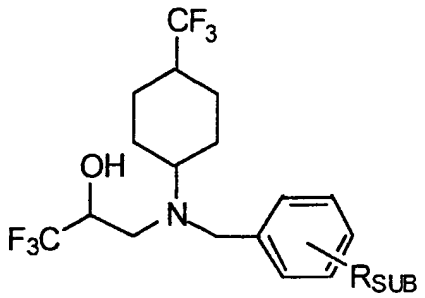
Example Table 5. (cont.). 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB}
513	3-OCF_3
514	3-OCF_2CF_2H
515	2-F, 5-CF_3
516	2-F, 4-CF_3
517	3-CF_3, 4-F
518	3-CF_3CF_2
519	3-cyclopentyl
520	3-isopropoxy
521	3-SCF_3
522	3-*sec*-butoxy
523	3-$C(CF_3)_2OH$
524	3-(2-furyl)
525	3-(3-furyl)
526	3-isobutyl
527	3-isobutoxy
528	3-ethoxy
529	3-OCH_2CF_3
530	3-propoxy
531	3-*tert*-butoxy

Ex. No.	R_{SUB}
532	3-(2-thienyl)
533	3-cyclopropyl
534	4-F, 3-(2-furyl)
535	3-(3-CF_3-phenoxy)
536	3,4-(OCF_2CF_2O)
537	3-OCF_2CF_3
538	3-cyclopentoxy
539	3-(cyclopropyl)methoxy
540	3-$OCH_2CH(OH)CF_3$
541	3-CF_3
542	4-CF_3
543	3-$CH_2CF_2CF_3$
544	3-CH_2CF_3
545	3-$CH(CF_3)_2$
546	3-$CF_2CF_2CF_3$
547	3-phenoxy
548	3-phenyl
549	3-(tetrahydro-2-furyl)
550	isoamyl

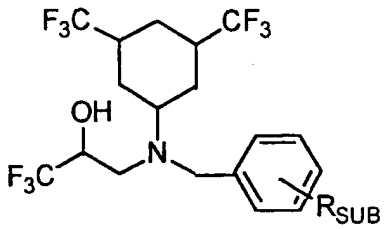
Example Table 5. (cont.). 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB}
551	3-OCF_3
552	3-OCF_2CF_2H
553	2-F, 5-CF_3
554	2-F, 4-CF_3
555	3-CF_3, 4-F
556	3-CF_3CF_2
557	3-cyclopentyl
558	3-isopropoxy
559	3-SCF_3
560	3-*sec*-butoxy
561	3-$C(CF_3)_2OH$
562	3-(2-furyl)
563	3-(3-furyl)
564	3-isobutyl
565	3-isobutoxy
566	3-ethoxy
567	3-OCH_2CF_3
568	3-propoxy
569	3-*tert*-butoxy

Ex. No.	R_{SUB}
570	3-(2-thienyl)
571	3-cyclopropyl
572	4-F, 3-(2-furyl)
573	3-(3-CF_3-phenoxy)
574	3,4-(OCF_2CF_2O)
575	3-OCF_2CF_3
576	3-cyclopentoxy
577	3-(cyclopropyl)methoxy
578	3-$OCH_2CH(OH)CF_3$
579	3-CF_3
580	4-CF_3
581	3-$CH_2CF_2CF_3$
582	3-CH_2CF_3
583	3-$CH(CF_3)_2$
584	3-$CF_2CF_2CF_3$
585	3-phenoxy
586	3-phenyl
587	3-(tetrahydro-2-furyl)
588	isoamyl

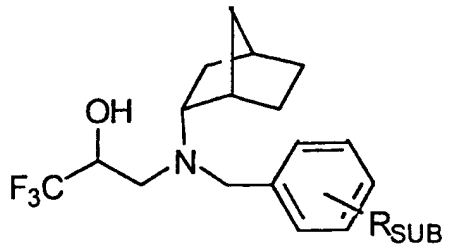
Example Table 5. (cont.). 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB}
589	3-OCF_3
590	3-OCF_2CF_2H
591	2-F, 5-CF_3
592	2-F, 4-CF_3
593	3-CF_3, 4-F
594	3-CF_3CF_2
595	3-cyclopentyl
596	3-isopropoxy
597	3-SCF_3
598	3-*sec*-butoxy
599	3-$C(CF_3)_2OH$
600	3-(2-furyl)
601	3-(3-furyl)
602	3-isobutyl
603	3-isobutoxy
604	3-ethoxy
605	3-OCH_2CF_3
606	3-propoxy
607	3-*tert*-butoxy

Ex. No.	R_{SUB}
608	3-(2-thienyl)
609	3-cyclopropyl
610	4-F, 3-(2-furyl)
611	3-(3-CF_3-phenoxy)
612	3,4-(OCF_2CF_2O)
613	3-OCF_2CF_3
614	3-cyclopentoxy
615	3-(cyclopropyl)methoxy
616	3-$OCH_2CH(OH)CF_3$
617	3-CF_3
618	4-CF_3
619	3-$CH_2CF_2CF_3$
620	3-CH_2CF_3
621	3-$CH(CF_3)_2$
622	3-$CF_2CF_2CF_3$
623	3-phenoxy
624	3-phenyl
625	3-(tetrahydro-2-furyl)
626	isoamyl

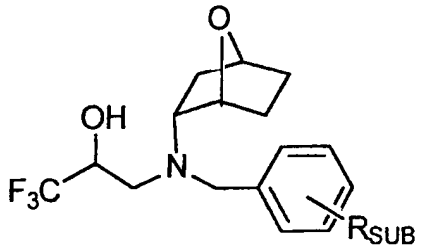
Example Table 5. (cont.). 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB}
627	3-OCF_3
628	3-OCF_2CF_2H
629	2-F, 5-CF_3
630	2-F, 4-CF_3
631	3-CF_3, 4-F
632	3-CF_3CF_2
633	3-cyclopentyl
634	3-isopropoxy
635	3-SCF_3
636	3-*sec*-butoxy
637	3-$C(CF_3)_2OH$
638	3-(2-furyl)
639	3-(3-furyl)
640	3-isobutyl
641	3-isobutoxy
642	3-ethoxy
643	3-OCH_2CF_3
644	3-propoxy
645	3-*tert*-butoxy

Ex. No.	R_{SUB}
646	3-(2-thienyl)
647	3-cyclopropyl
648	4-F, 3-(2-furyl)
649	3-(3-CF_3-phenoxy)
650	3,4-(OCF_2CF_2O)
651	3-OCF_2CF_3
652	3-cyclopentoxy
653	3-(cyclopropyl)methoxy
654	3-$OCH_2CH(OH)CF_3$
655	3-CF_3
656	4-CF_3
657	3-$CH_2CF_2CF_3$
658	3-CH_2CF_3
659	3-$CH(CF_3)_2$
660	3-$CF_2CF_2CF_3$
661	3-phenoxy
662	3-phenyl
663	3-(tetrahydro-2-furyl)
664	isoamyl

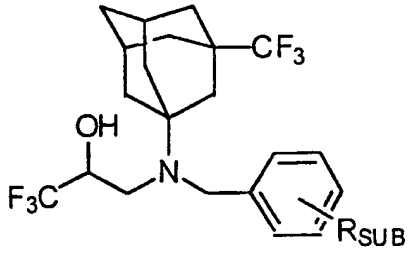
Example Table 5. (cont.). 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB}
665	3-OCF_3
666	3-OCF_2CF_2H
667	2-F, 5-CF_3
668	2-F, 4-CF_3
669	3-CF_3, 4-F
670	3-CF_3CF_2
671	3-cyclopentyl
672	3-isopropoxy
673	3-SCF_3
674	3-*sec*-butoxy
675	3-$C(CF_3)_2OH$
676	3-(2-furyl)
677	3-(3-furyl)
678	3-isobutyl
679	3-isobutoxy
680	3-ethoxy
681	3-OCH_2CF_3
682	3-propoxy
683	3-*tert*-butoxy

Ex. No.	R_{SUB}
684	3-(2-thienyl)
685	3-cyclopropyl
686	4-F, 3-(2-furyl)
687	3-(3-CF_3-phenoxy)
688	3,4-(OCF_2CF_2O)
689	3-OCF_2CF_3
690	3-cyclopentoxy
691	3-(cyclopropyl)methoxy
692	3-$OCH_2CH(OH)CF_3$
693	3-CF_3
694	4-CF_3
695	3-$CH_2CF_2CF_3$
696	3-CH_2CF_3
697	3-$CH(CF_3)_2$
698	3-$CF_2CF_2CF_3$
699	3-phenoxy
700	3-phenyl
701	3-(tetrahydro-2-furyl)
702	isoamyl

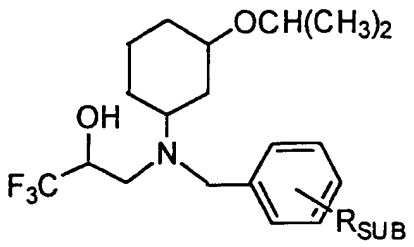
Example Table 5. (cont.). 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB}
703	3-OCF_3
704	3-OCF_2CF_2H
705	2-F, 5-CF_3
706	2-F, 4-CF_3
707	3-CF_3, 4-F
708	3-CF_3CF_2
709	3-cyclopentyl
710	3-isopropoxy
711	3-SCF_3
712	3-*sec*-butoxy
713	3-$C(CF_3)_2OH$
714	3-(2-furyl)
715	3-(3-furyl)
716	3-isobutyl
717	3-isobutoxy
718	3-ethoxy
719	3-OCH_2CF_3
720	3-propoxy
721	3-*tert*-butoxy

Ex. No.	R_{SUB}
722	3-(2-thienyl)
723	3-cyclopropyl
724	4-F, 3-(2-furyl)
725	3-(3-CF_3-phenoxy)
726	3,4-(OCF_2CF_2O)
727	3-OCF_2CF_3
728	3-cyclopentoxy
729	3-(cyclopropyl)methoxy
730	3-$OCH_2CH(OH)CF_3$
731	3-CF_3
732	4-CF_3
733	3-$CH_2CF_2CF_3$
734	3-CH_2CF_3
735	3-$CH(CF_3)_2$
736	3-$CF_2CF_2CF_3$
737	3-phenoxy
738	3-phenyl
739	3-(tetrahydro-2-furyl)
740	isoamyl

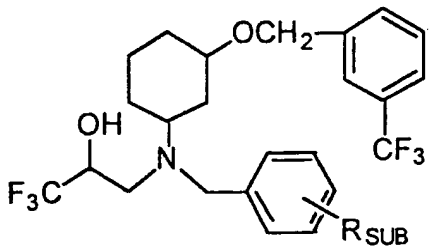
Example Table 5. (cont.). 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB}
741	3-OCF_3
742	3-OCF_2CF_2H
743	2-F, 5-CF_3
744	2-F, 4-CF_3
745	3-CF_3, 4-F
746	3-CF_3CF_2
747	3-cyclopentyl
748	3-isopropoxy
749	3-SCF_3
750	3-*sec*-butoxy
751	3-$C(CF_3)_2OH$
752	3-(2-furyl)
753	3-(3-furyl)
754	3-isobutyl
755	3-isobutoxy
756	3-ethoxy
757	3-OCH_2CF_3
758	3-propoxy
759	3-*tert*-butoxy

Ex. No.	R_{SUB}
760	3-(2-thienyl)
761	3-cyclopropyl
762	4-F, 3-(2-furyl)
763	3-(3-CF_3-phenoxy)
764	3,4-(OCF_2CF_2O)
765	3-OCF_2CF_3
766	3-cyclopentoxy
767	3-(cyclopropyl)methoxy
768	3-$OCH_2CH(OH)CF_3$
769	3-CF_3
770	4-CF_3
771	3-$CH_2CF_2CF_3$
772	3-CH_2CF_3
773	3-$CH(CF_3)_2$
774	3-$CF_2CF_2CF_3$
775	3-phenoxy
776	3-phenyl
777	3-(tetrahydro-2-furyl)
778	isoamyl

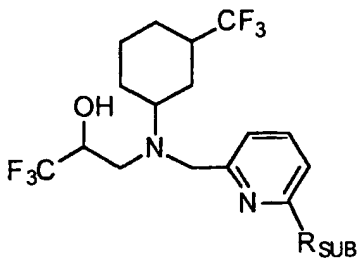
Example Table 5. (cont.). 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB}
779	3-OCF_3
780	3-OCF_2CF_2H
781	2-F, 5-CF_3
782	2-F, 4-CF_3
783	3-CF_3, 4-F
784	3-CF_3CF_2
785	3-cyclopentyl
786	3-isopropoxy
787	3-SCF_3
788	3-*sec*-butoxy
789	3-$C(CF_3)_2OH$
790	3-(2-furyl)
791	3-(3-furyl)
792	3-isobutyl
793	3-isobutoxy
794	3-ethoxy
795	3-OCH_2CF_3
796	3-propoxy
797	3-*tert*-butoxy

Ex. No.	R_{SUB}
798	3-(2-thienyl)
799	3-cyclopropyl
800	4-F, 3-(2-furyl)
801	3-(3-CF_3-phenoxy)
802	3,4-(OCF_2CF_2O)
803	3-OCF_2CF_3
804	3-cyclopentoxy
805	3-(cyclopropyl)methoxy
806	3-$OCH_2CH(OH)CF_3$
807	3-CF_3
808	4-CF_3
809	3-$CH_2CF_2CF_3$
810	3-CH_2CF_3
811	3-$CH(CF_3)_2$
812	3-$CF_2CF_2CF_3$
813	3-phenoxy
814	3-phenyl
815	3-(tetrahydro-2-furyl)
816	isoamyl

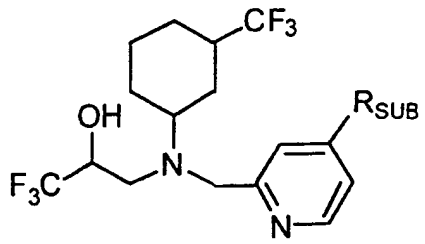
Example Table 5. (cont.). 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB}
817	OCF_3
818	OCF_2CF_2H
819	OCF_2CF_3
820	CH_2CF_3
821	CF_3
822	CF_3CF_2
823	cyclopentyl
824	isopropoxy
825	SCF_3
826	*sec*-butoxy
827	$C(CF_3)_2OH$
828	(2-furyl)
829	(3-furyl)
830	isobutyl
831	isobutoxy
832	ethoxy
833	OCH_2CF_3

Ex. No.	R_{SUB}
834	(2-thienyl)
835	cyclopropyl
836	(3-CF_3-phenoxy)
837	cyclopentoxy
838	(cyclopropyl)methoxy
839	$OCH_2CH(OH)CF_3$
840	$CH_2CF_2CF_3$
841	$CH(CF_3)_2$
842	$CH(CF_3)_2$
843	$CF_2CF_2CF_3$
844	phenoxy
845	phenyl
846	(tetrahydro-2-furyl)
847	isoamyl
848	propoxy
849	*tert*-butoxy
850	(2-pyridyl)

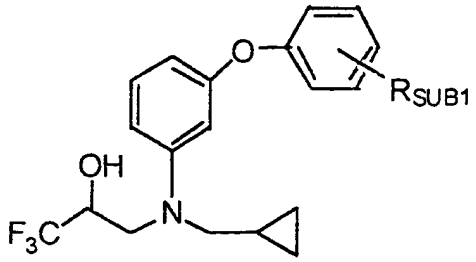
Example Table 5. (cont.). 3-[(*N*-cycloalkyl)[[aryl]methyl]amino]-halo-2-propanols.

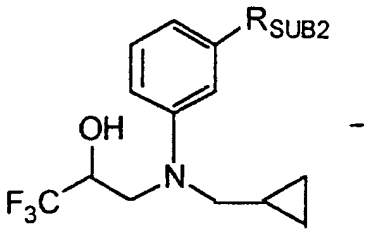


Ex. No.	R_{SUB}
851	OCF_3
852	OCF_2CF_2H
853	OCF_2CF_3
854	CH_2CF_3
855	CF_3
856	CF_3CF_2
857	cyclopentyl
858	isopropoxy
859	SCF_3
860	*sec*-butoxy
861	$C(CF_3)_2OH$
862	(2-furyl)
863	(3-furyl)
864	isobutyl
865	isobutoxy
866	ethoxy
867	OCH_2CF_3

Ex. No.	R_{SUB}
868	(2-thienyl)
869	cyclopropyl
870	(3-CF_3-phenoxy)
871	cyclopentoxy
872	(cyclopropyl)methoxy
873	$OCH_2CH(OH)CF_3$
874	$CH_2CF_2CF_3$
875	$CH(CF_3)_2$
876	$CH(CF_3)_2$
877	$CF_2CF_2CF_3$
878	phenoxy
879	phenyl
880	(tetrahydro-2-furyl)
881	isoamyl
882	propoxy
883	*tert*-butoxy
884	(2-pyridyl)

Example Table 6. 3-[(*N*-aryl)[[cycloalkyl]methyl]amino]-halo-2-propanols.





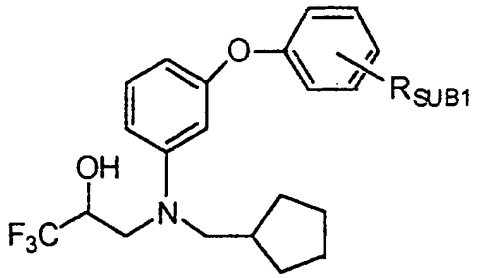
Ex. No.	R_{SUB1}
885	3-isopropyl
886	2-Cl, 3-Cl
887	3-CF_3O
888	4-F
889	4-CH_3
890	2-F, 5-Br
891	4-Cl, 3-CH_3CH_2
892	3-CH_3CH_2
893	3-CH_3, 5-CH_3
894	3-$(CH_3)_3C$
895	4-F, 3-CH_3
896	3-Cl, 4-Cl
897	3,4-$(CH_2)_4$
898	3-HCF_2CF_2O
899	3-CHF_2O
900	3-$(CH_3)_2N$
901	3-cyclopropyl
902	3-(2-furyl)
903	3-CF_3CF_2
904	4-NH_2
905	3-CH_3, 4-CH_3, 5-CH_3
906	4-$CH_3CH_2CH_2O$

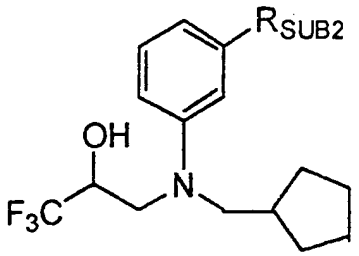
Ex. No.	R_{SUB2}
909	3-CF_3O-benzyloxy
910	3-CF_3-benzyloxy
911	3-F, 5-F-benzyloxy
912	cyclohexylmethyleneoxy
913	benzyloxy
914	3-CF_3, 5-CF_3-benzyloxy
915	4-CF_3O-benzyloxy
916	4-CH_3CH_2-benzyloxy
917	isopropoxy
918	3-CF_3-benzyl
919	isopropylthio
920	cyclopentoxy
921	3-Cl-5-pyridinyloxy
922	3-CF_3S-benzyloxy
923	3-CH_3, 4-CH_3-benzyloxy
924	2-F, 3-CF_3-benzyloxy
925	3-F, 5-CF_3-benzyloxy
926	4-$(CH_3)_2CH$-benzyloxy
927	1-phenylethoxy
928	4-F, 3-CH_3-benzoyl
929	3-CF_3-phenyl
930	4-CH_3O-phenylamino

Ex. No.	R_{SUB1}
907	3-CF_3
908	2-NO_2

Ex. No.	R_{SUB2}
931	cyclopropoxy
932	4-NO_2-phenylthio

Example Table 6 (cont.). 3-[(*N*-aryl)[[cycloalkyl]methyl]amino]-halo-2-propanols.





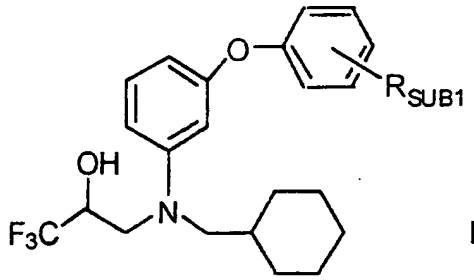
Ex. No.	R_{SUB1}
933	3-isopropyl
934	2-Cl, 3-Cl
935	3-CF_3O
936	4-F
937	4-CH_3
938	2-F, 5-Br
939	4-Cl, 3-CH_3CH_2
940	3-CH_3CH_2
941	3-CH_3, 5-CH_3
942	3-$(CH_3)_3C$
943	4-F, 3-CH_3
944	3-Cl, 4-Cl
945	3,4-$(CH_2)_4$
946	3-HCF_2CF_2O
947	3-CHF_2O
948	3-$(CH_3)_2N$
949	3-cyclopropyl

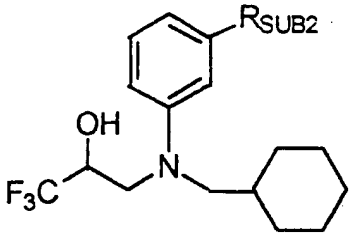
Ex. No.	R_{SUB2}
957	3-CF_3O-benzyloxy
958	3-CF_3-benzyloxy
959	3-F, 5-F-benzyloxy
960	cyclohexylmethyleneoxy
961	benzyloxy
962	3-CF_3, 5-CF_3-benzyloxy
963	4-CF_3O-benzyloxy
964	4-CH_3CH_2-benzyloxy
965	isopropoxy
966	3-CF_3-benzyl
967	isopropylthio
968	cyclopentoxy
969	3-Cl-5-pyridinyloxy
970	3-CF_3S-benzyloxy
971	3-CH_3, 4-CH_3-benzyloxy
972	2-F, 3-CF_3-benzyloxy
973	3-F, 5-CF_3-benzyloxy

Ex. No.	R_{SUB1}
950	3-(2-furyl)
951	3-CF_3CF_2
952	4-NH_2
953	3-CH_3, 4-CH_3, 5-CH_3
954	4-$CH_3CH_2CH_2O$
955	3-CF_3
956	2-NO_2

Ex. No.	R_{SUB2}
974	4-$(CH_3)_2CH$-benzyloxy
975	1-phenylethoxy
976	4-F, 3-CH_3-benzoyl
977	3-CF_3-phenyl
978	4-CH_3O-phenylamino
979	cyclopropoxy
980	4-NO_2-phenylthio

Example Table 6 (cont.). 3-[(*N*-aryl)[[cycloalkyl]methyl]amino]-halo-2-propanols.





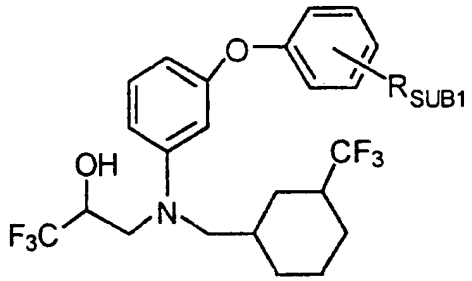
Ex. No.	R_{SUB1}
981	3-isopropyl
982	2-Cl, 3-Cl
983	3-CF_3O
984	4-F
985	4-CH_3
986	2-F, 5-Br
987	4-F, 3-CF_3
988	3-CH_3CH_2
989	3-CH_3, 5-CH_3
990	3-$(CH_3)_3C$
991	4-F, 3-CH_3

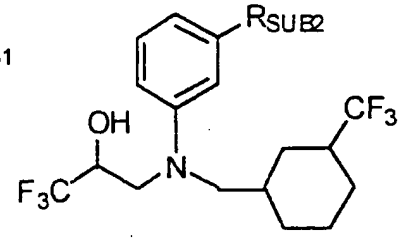
Ex. No.	R_{SUB2}
1005	3-CF_3O-benzyloxy
1006	3-CF_3-benzyloxy
1007	3-F, 5-F-benzyloxy
1008	cyclohexylmethyleneoxy
1009	benzyloxy
1010	3-CF_3, 5-CF_3-benzyloxy
1011	4-CF_3O-benzyloxy
1012	4-CH_3CH_2-benzyloxy
1013	isopropoxy
1014	3-CF_3-benzyl
1015	isopropylthio

Ex. No.	R_{SUB1}
992	3-Cl, 4-Cl
993	3,4-$(CH_2)_4$
994	3-HCF_2CF_2O
995	3-CHF_2O
996	3-$(CH_3)_2N$
997	3-cyclopropyl
998	3-(2-furyl)
999	3-CF_3CF_2
1000	4-NH_2
1001	3-CH_3, 4-CH_3, 5-CH_3
1002	4-$CH_3CH_2CH_2O$
1003	3-CF_3
1004	2-NO_2

Ex. No.	R_{SUB2}
1016	cyclopentoxy
1017	3-Cl-5-pyridinyloxy
1018	3-CF_3S-benzyloxy
1019	3-CH_3, 4-CH_3-benzyloxy
1020	2-F, 3-CF_3-benzyloxy
1021	3-F, 5-CF_3-benzyloxy
1022	4-$(CH_3)_2CH$-benzyloxy
1023	1-phenylethoxy
1024	4-F, 3-CH_3-benzoyl
1025	3-CF_3-phenyl
1026	4-CH_3O-phenylamino
1027	cyclopropoxy
1028	4-NO_2-phenylthio

Example Table 6 (cont.). 3-[(*N*-aryl)[[cycloalkyl]methyl]amino]-halo-2-propanols.





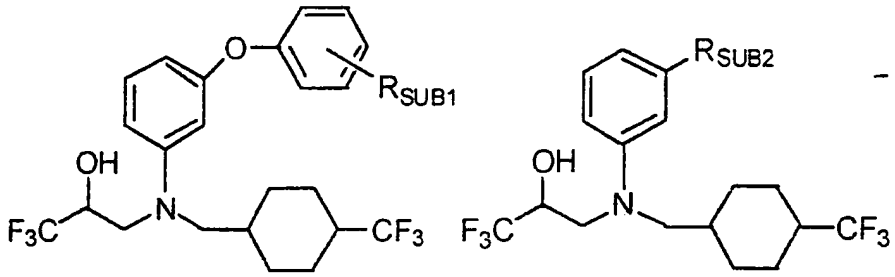
Ex. No.	R_{SUB1}
1029	3-isopropyl
1030	2-Cl, 3-Cl
1031	3-CF_3O
1032	4-F
1033	4-CH_3

Ex. No.	R_{SUB2}
1053	3-CF_3O-benzyloxy
1054	3-CF_3-benzyloxy
1055	3-F, 5-F-benzyloxy
1056	cyclohexylmethyleneoxy
1057	benzyloxy

Ex. No.	R_{SUB1}
1034	2-F, 5-Br
1035	4-Cl, 3-CH_3CH_2
1036	3-CH_3CH_2
1037	3-CH_3, 5-CH_3
1038	3-$(CH_3)_3C$
1039	4-F, 3-CH_3
1040	3-Cl, 4-Cl
1041	3,4-$(CH_2)_4$
1042	3-HCF_2CF_2O
1043	3-CHF_2O
1044	3-$(CH_3)_2N$
1045	3-cyclopropyl
1046	3-(2-furyl)
1047	3-CF_3CF_2
1048	4-NH_2
1049	3-CH_3, 4-CH_3, 5-CH_3
1050	4-$CH_3CH_2CH_2O$
1051	3-CF_3
1052	2-NO_2

Ex. No.	R_{SUB2}
1058	3-CF_3, 5-CF_3-benzyloxy
1059	4-CF_3O-benzyloxy
1060	4-CH_3CH_2-benzyloxy
1061	isopropoxy
1062	3-CF_3-benzyl
1063	isopropylthio
1064	cyclopentoxy
1065	3-Cl-5-pyridinyloxy
1066	3-CF_3S-benzyloxy
1067	3-CH_3, 4-CH_3-benzyloxy
1068	2-F, 3-CF_3-benzyloxy
1069	3-F, 5-CF_3-benzyloxy
1070	4-$(CH_3)_2CH$-benzyloxy
1071	1-phenylethoxy
1072	4-F, 3-CH_3-benzoyl
1073	3-CF_3-phenyl
1074	4-CH_3O-phenylamino
1075	cyclopropoxy
1076	4-NO_2-phenylthio

Example Table 6 (cont.). 3-[(*N*-aryl)[[cycloalkyl]methyl]amino]-halo-2-propanols.



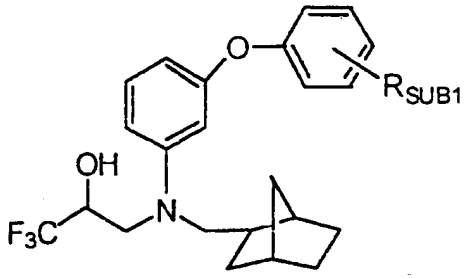
Ex. No.	R_{SUB1}
1077	3-isopropyl
1078	2-Cl, 3-Cl
1079	3-CF_3O
1080	4-F
1081	4-CH_3
1082	2-F, 5-Br
1083	4-Cl, 3-CH_3CH_2
1084	3-CH_3CH_2
1085	3-CH_3, 5-CH_3
1086	3-$(CH_3)_3C$
1087	4-F, 3-CH_3
1088	3-Cl, 4-Cl
1089	3,4-$(CH_2)_4$
1090	3-HCF_2CF_2O
1091	3-CHF_2O
1092	3-$(CH_3)_2N$
1093	3-cyclopropyl
1094	3-(2-furyl)
1095	3-CF_3CF_2
1096	4-NH_2
1097	3-CH_3, 4-CH_3, 5-CH_3

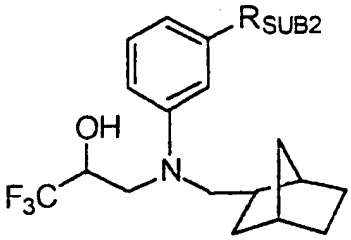
Ex. No.	R_{SUB2}
1101	3-CF_3O-benzyloxy
1102	3-CF_3-benzyloxy
1103	3-F, 5-F-benzyloxy
1104	cyclohexylmethyleneoxy
1105	benzyloxy
1106	3-CF_3, 5-CF_3-benzyloxy
1107	4-CF_3O-benzyloxy
1108	4-CH_3CH_2-benzyloxy
1109	isopropoxy
1110	3-CF_3-benzyl
1111	isopropylthio
1112	cyclopentoxy
1113	3-Cl-5-pyridinyloxy
1114	3-CF_3S-benzyloxy
1115	3-CH_3, 4-CH_3-benzyloxy
1116	2-F, 3-CF_3-benzyloxy
1117	3-F, 5-CF_3-benzyloxy
1118	4-$(CH_3)_2CH$-benzyloxy
1119	1-phenylethoxy
1120	4-F, 3-CH_3-benzoyl
1121	3-CF_3-phenyl

Ex. No.	R_{SUB1}
1098	4-$CH_3CH_2CH_2O$
1099	3-CF_3
1100	2-NO_2

Ex. No.	R_{SUB2}
1122	4-CH_3O-phenylamino
1123	cyclopropoxy
1124	4-NO_2-phenylthio

Example Table 6 (cont.). 3-[(*N*-aryl)[[cycloalkyl]methyl]amino]-halo-2-propanols.





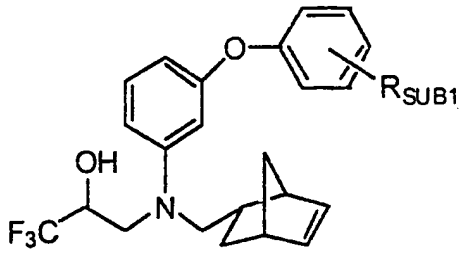
Ex. No.	R_{SUB1}
1125	3-isopropyl
1126	2-Cl, 3-Cl
1127	3-CF_3O
1128	4-F
1129	4-CH_3
1130	2-F, 5-Br
1131	4-Cl, 3-CH_3CH_2
1132	3-CH_3CH_2
1133	3-CH_3, 5-CH_3
1134	3-$(CH_3)_3C$
1135	4-F, 3-CH_3
1136	3-Cl, 4-Cl
1137	3,4-$(CH_2)_4$
1138	3-HCF_2CF_2O
1139	3-CHF_2O

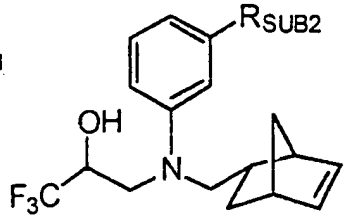
Ex. No.	R_{SUB2}
1149	3-CF_3O-benzyloxy
1150	3-CF_3-benzyloxy
1151	3-F, 5-F-benzyloxy
1152	cyclohexylmethyleneoxy
1153	benzyloxy
1154	3-CF_3, 5-CF_3-benzyloxy
1155	4-CF_3O-benzyloxy
1156	4-CH_3CH_2-benzyloxy
1157	isopropoxy
1158	3-CF_3-benzyl
1159	isopropylthio
1160	cyclopentoxy
1161	3-Cl-5-pyridinyloxy
1162	3-CF_3S-benzyloxy
1163	3-CH_3, 4-CH_3-benzyloxy

Ex. No.	R_{SUB1}
1140	3-$(CH_3)_2N$
1141	3-cyclopropyl
1142	3-(2-furyl)
1143	3-CF_3CF_2
1144	4-NH_2
1145	3-CH_3, 4-CH_3, 5-CH_3
1146	4-$CH_3CH_2CH_2O$
1147	3-CF_3
1148	2-NO_2

Ex. No.	R_{SUB2}
1164	2-F, 3-CF_3-benzyloxy
1165	3-F, 5-CF_3-benzyloxy
1166	4-$(CH_3)_2CH$-benzyloxy
1167	1-phenylethoxy
1168	4-F, 3-CH_3-benzoyl
1169	3-CF_3-phenyl
1170	4-CH_3O-phenylamino
1171	cyclopropoxy
1172	4-NO_2-phenylthio

Example Table 6 (cont.). 3-[(*N*-aryl)[[cycloalkyl]methyl]amino]-halo-2-propanols.





Ex. No.	R_{SUB1}
1173	3-isopropyl
1174	2-Cl, 3-Cl
1175	3-CF_3O
1176	4-F
1177	4-CH_3
1178	2-F, 5-Br
1179	4-Cl, 3-CH_3CH_2
1180	3-CH_3CH_2
1181	3-CH_3, 5-CH_3

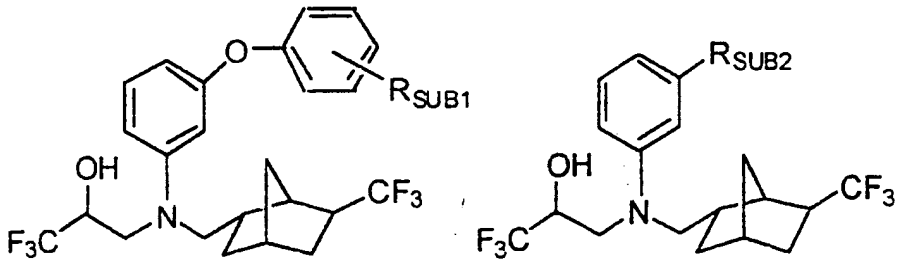
Ex. No.	R_{SUB2}
1197	3-CF_3O-benzyloxy
1198	3-CF_3-benzyloxy
1199	3-F, 5-F-benzyloxy
1200	cyclohexylmethyleneoxy
1201	benzyloxy
1202	3-CF_3, 5-CF_3-benzyloxy
1203	4-CF_3O-benzyloxy
1204	4-CH_3CH_2-benzyloxy
1205	isopropoxy

Ex. No.	R_{SUB1}
1182	3-$(CH_3)_3C$
1183	4-F, 3-CH_3
1184	3-Cl, 4-Cl
1185	3.4-$(CH_2)_4$
1186	3-HCF_2CF_2O
1187	3-CHF_2O
1188	3-$(CH_3)_2N$
1189	3-cyclopropyl
1190	3-(2-furyl)
1191	3-CF_3CF_2
1192	4-NH_2
1193	3-CH_3, 4-CH_3, 5-CH_3
1194	4-$CH_3CH_2CH_2O$
1195	3-CF_3
1196	2-NO_2

Ex. No.	R_{SUB2}
1206	3-CF_3-benzyl
1207	isopropylthio
1208	cyclopentoxy
1209	3-Cl-5-pyridinyloxy
1210	3-CF_3S-benzyloxy
1211	3-CH_3, 4-CH_3-benzyloxy
1212	2-F, 3-CF_3-benzyloxy
1213	3-F, 5-CF_3-benzyloxy
1214	4-$(CH_3)_2CH$-benzyloxy
1215	1-phenylethoxy
1216	4-F, 3-CH_3-benzoyl
1217	3-CF_3-phenyl
1218	4-CH_3O-phenylamino
1219	cyclopropoxy
1220	4-NO_2-phenylthio

5

Example Table 6 (cont.). 3-[(*N*-aryl)[[cycloalkyl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB1}
1221	3-isopropyl
1222	2-Cl, 3-Cl

Ex. No.	R_{SUB2}
1245	3-CF_3O-benzyloxy
1246	3-CF_3-benzyloxy

Ex. No.	R_{SUB1}
1223	3-CF_3O
1224	4-F
1225	4-CH_3
1226	2-F, 5-Br
1227	4-Cl, 3-CH_3CH_2
1228	3-CH_3CH_2
1229	3-CH_3, 5-CH_3
1230	3-$(CH_3)_3C$
1231	4-F, 3-CH_3
1232	3-Cl, 4-Cl
1233	3,4-$(CH_2)_4$
1234	3-HCF_2CF_2O
1235	3-CHF_2O
1236	3-$(CH_3)_2N$
1237	3-cyclopropyl
1238	3-(2-furyl)
1239	3-CF_3CF_2
1240	4-NH_2
1241	3-CH_3, 4-CH_3, 5-CH_3
1242	4-$CH_3CH_2CH_2O$
1243	3-CF_3
1244	2-NO_2

Ex. No.	R_{SUB2}
1247	3-F, 5-F-benzyloxy
1248	cyclohexylmethyleneoxy
1249	benzyloxy
1250	3-CF_3, 5-CF_3-benzyloxy
1251	4-CF_3O-benzyloxy
1252	4-CH_3CH_2-benzyloxy
1253	isopropoxy
1254	3-CF_3-benzyl
1255	isopropylthio
1256	cyclopentoxy
1257	3-Cl-5-pyridinyloxy
1258	3-CF_3S-benzyloxy
1259	3-CH_3, 4-CH_3-benzyloxy
1260	2-F, 3-CF_3-benzyloxy
1261	3-F, 5-CF_3-benzyloxy
1262	4-$(CH_3)_2CH$-benzyloxy
1263	1-phenylethoxy
1264	4-F, 3-CH_3-benzoyl
1265	3-CF_3-phenyl
1266	4-CH_3O-phenylamino
1267	cyclopropoxy
1268	4-NO_2-phenylthio

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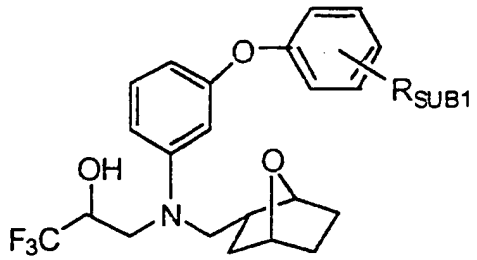
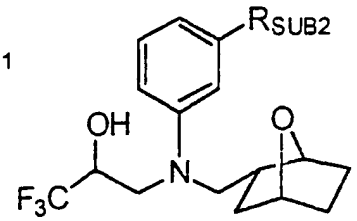
Example Table 6 (cont.). 3-[(*N*-aryl)[[cycloalkyl]methyl]amino]-halo-2-propanols.





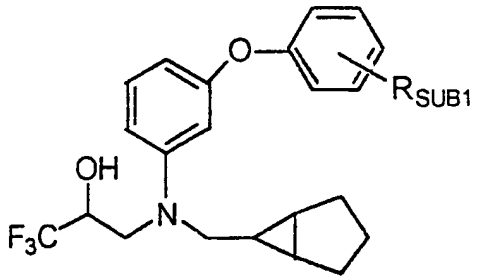
Ex. No.	R_{SUB1}
1269	3-isopropyl
1270	2-Cl, 3-Cl
1271	3-CF_3O
1272	4-F
1273	4-CH_3
1274	2-F, 5-Br
1275	4-Cl, 3-CH_3CH_2
1276	3-CH_3CH_2
1277	3-CH_3, 5-CH_3
1278	3-$(CH_3)_3C$
1279	4-F, 3-CH_3
1280	3-Cl, 4-Cl
1281	3,4-$(CH_2)_4$
1282	3-HCF_2CF_2O
1283	3-CHF_2O
1284	3-$(CH_3)_2N$
1285	3-cyclopropyl
1286	3-(2-furyl)
1287	3-CF_3CF_2
1288	4-NH_2
1289	3-CH_3, 4-CH_3, 5-CH_3

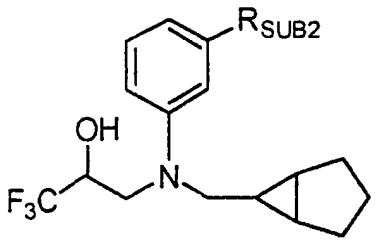
Ex. No.	R_{SUB2}
1293	3-CF_3O-benzyloxy
1294	3-CF_3-benzyloxy
1295	3-F, 5-F-benzyloxy
1296	cyclohexylmethyleneoxy
1297	benzyloxy
1298	3-CF_3, 5-CF_3-benzyloxy
1299	4-CF_3O-benzyloxy
1300	4-CH_3CH_2-benzyloxy
1301	isopropoxy
1302	3-CF_3-benzyl
1303	isopropylthio
1304	cyclopentoxy
1305	3-Cl-5-pyridinyloxy
1306	3-CF_3S-benzyloxy
1307	3-CH_3, 4-CH_3-benzyloxy
1308	2-F, 3-CF_3-benzyloxy
1309	3-F, 5-CF_3-benzyloxy
1310	4-$(CH_3)_2CH$-benzyloxy
1311	1-phenylethoxy
1312	4-F, 3-CH_3-benzoyl
1313	3-CF_3-phenyl

Ex. No.	R_{SUB1}
1290	4-$CH_3CH_2CH_2O$
1291	3-CF_3
1292	2-NO_2

Ex. No.	R_{SUB2}
1314	4-CH_3O-phenylamino
1315	cyclopropoxy
1316	4-NO_2-phenylthio

Example Table 6 (cont.). 3-[(*N*-aryl)[[cycloalkyl]methyl]amino]-halo-2-propanols.





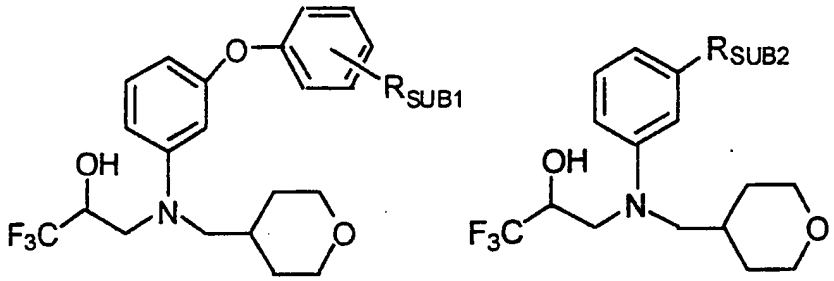
Ex. No.	R_{SUB1}
1317	3-isopropyl
1318	2-Cl, 3-Cl
1319	3-CF_3O
1320	4-F
1321	4-CH_3
1322	2-F, 5-Br
1323	4-Cl, 3-CH_3CH_2
1324	3-CH_3CH_2
1325	3-CH_3, 5-CH_3
1326	3-$(CH_3)_3C$
1327	4-F, 3-CH_3
1328	3-Cl, 4-Cl
1329	3,4-$(CH_2)_4$
1330	3-HCF_2CF_2O
1331	3-CHF_2O

Ex. No.	R_{SUB2}
1341	3-CF_3O-benzyloxy
1342	3-CF_3-benzyloxy
1343	3-F, 5-F-benzyloxy
1344	cyclohexylmethyleneoxy
1345	benzyloxy
1346	3-CF_3, 5-CF_3-benzyloxy
1347	4-CF_3O-benzyloxy
1348	4-CH_3CH_2-benzyloxy
1349	isopropoxy
1350	3-CF_3-benzyl
1351	isopropylthio
1352	cyclopentoxy
1353	3-Cl-5-pyridinyloxy
1354	3-CF_3S-benzyloxy
1355	3-CH_3, 4-CH_3-benzyloxy

Ex. No.	R_{SUB1}
1332	3-$(CH_3)_2N$
1333	3-cyclopropyl
1334	3-(2-furyl)
1335	3-CF_3CF_2
1336	4-NH_2
1337	3-CH_3, 4-CH_3, 5-CH_3
1338	4-$CH_3CH_2CH_2O$
1339	3-CF_3
1340	2-NO_2

Ex. No.	R_{SUB2}
1356	2-F, 3-CF_3-benzyloxy
1357	3-F, 5-CF_3-benzyloxy
1358	4-$(CH_3)_2CH$-benzyloxy
1359	1-phenylethoxy
1360	4-F, 3-CH_3-benzoyl
1361	3-CF_3-phenyl
1362	4-CH_3O-phenylamino
1363	cyclopropoxy
1364	4-NO_2-phenylthio

Example Table 6 (cont.). 3-[(*N*-aryl)[[cycloalkyl]methyl]amino]-halo-2-propanols.



Ex. No.	R_{SUB1}
1365	3-isopropyl
1366	2-Cl, 3-Cl
1367	3-CF_3O
1368	4-F
1369	4-CH_3
1370	2-F, 5-Br
1371	4-Cl, 3-CH_3CH_2
1372	3-CH_3CH_2
1373	3-CH_3, 5-CH_3

Ex. No.	R_{SUB2}
1389	3-CF_3O-benzyloxy
1390	3-CF_3-benzyloxy
1391	3-F, 5-F-benzyloxy
1392	cyclohexylmethyleneoxy
1393	benzyloxy
1394	3-CF_3, 5-CF_3-benzyloxy
1395	4-CF_3O-benzyloxy
1396	4-CH_3CH_2-benzyloxy
1397	isopropoxy

Ex. No.	R_{SUB1}
1374	3-$(CH_3)_3C$
1375	4-F, 3-CH_3
1376	3-Cl, 4-Cl
1377	3,4-$(CH_2)_4$
1378	3-HCF_2CF_2O
1379	3-CHF_2O
1380	3-$(CH_3)_2N$
1381	3-cyclopropyl
1382	3-(2-furyl)
1383	3-CF_3CF_2
1384	4-NH_2
1385	3-CH_3, 4-CH_3, 5-CH_3
1386	4-$CH_3CH_2CH_2O$
1387	3-CF_3
1388	2-NO_2

Ex. No.	R_{SUB2}
1398	3-CF_3-benzyl
1399	isopropylthio
1400	cyclopentoxy
1401	3-Cl-5-pyridinyloxy
1402	3-CF_3S-benzyloxy
1403	3-CH_3, 4-CH_3-benzyloxy
1404	2-F, 3-CF_3-benzyloxy
1405	3-F, 5-CF_3-benzyloxy
1406	4-$(CH_3)_2CH$-benzyloxy
1407	1-phenylethoxy
1408	4-F, 3-CH_3-benzoyl
1409	3-CF_3-phenyl
1410	4-CH_3O-phenylamino
1411	cyclopropoxy
1412	4-NO_2-phenylthio

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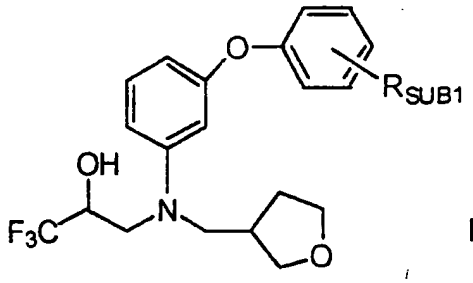
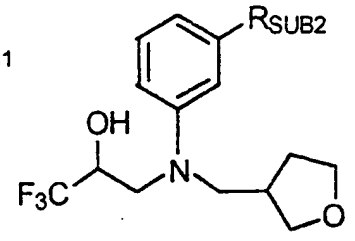
Example Table 6 (cont.). 3-[(*N*-aryl)[[cycloalkyl]methyl]amino]-halo-2-propanols.





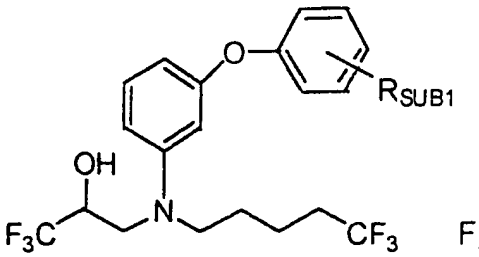
Ex. No.	R_{SUB1}
1413	3-isopropyl
1414	2-Cl, 3-Cl
1415	3-CF_3O

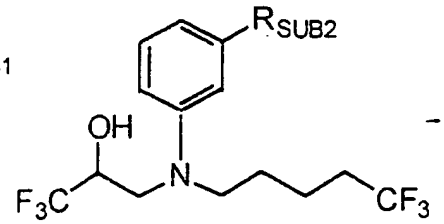
Ex. No.	R_{SUB2}
1437	3-CF_3O-benzyloxy
1438	3-CF_3-benzyloxy
1439	3-F, 5-F-benzyloxy

Ex. No.	R_{SUB1}
1416	4-F
1417	4-CH_3
1418	2-F, 5-Br
1419	4-Cl, 3-CH_3CH_2
1420	3-CH_3CH_2
1421	3-CH_3, 5-CH_3
1422	3-$(CH_3)_3C$
1423	4-F, 3-CH_3
1424	3-Cl, 4-Cl
1425	3,4-$(CH_2)_4$
1426	3-HCF_2CF_2O
1427	3-CHF_2O
1428	3-$(CH_3)_2N$
1429	3-cyclopropyl
1430	3-(2-furyl)
1431	3-CF_3CF_2
1432	4-NH_2
1433	3-CH_3, 4-CH_3, 5-CH_3
1434	4-$CH_3CH_2CH_2O$
1435	3-CF_3
1436	2-NO_2

Ex. No.	R_{SUB2}
1440	cyclohexylmethyleneoxy
1441	benzyloxy
1442	3-CF_3, 5-CF_3-benzyloxy
1443	4-CF_3O-benzyloxy
1444	4-CH_3CH_2-benzyloxy
1445	isopropoxy
1446	3-CF_3-benzyl
1447	isopropylthio
1448	cyclopentoxy
1449	3-Cl-5-pyridinyloxy
1450	3-CF_3S-benzyloxy
1451	3-CH_3, 4-CH_3-benzyloxy
1452	2-F, 3-CF_3-benzyloxy
1453	3-F, 5-CF_3-benzyloxy
1454	4-$(CH_3)_2CH$-benzyloxy
1455	1-phenylethoxy
1456	4-F, 3-CH_3-benzoyl
1457	3-CF_3-phenyl
1458	4-CH_3O-phenylamino
1459	cyclopropoxy
1460	4-NO_2-phenylthio

Example Table 7. 3-[(*N*-aryl)[[haloalkyl]methyl]amino]-halo-2-propanols.





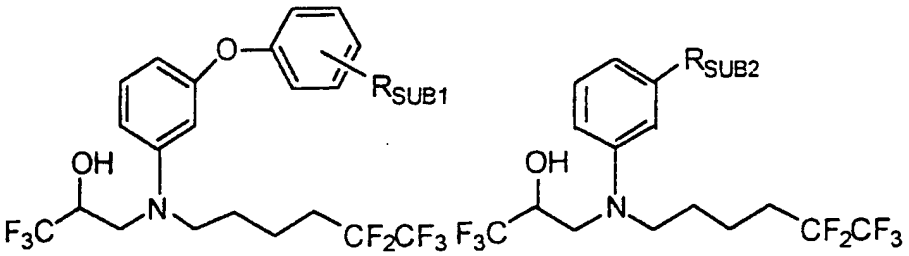
Ex. No.	R_{SUB1}
1461	3-isopropyl
1462	2-Cl, 3-Cl
1463	3-CF_3O
1464	4-F
1465	4-CH_3
1466	2-F, 5-Br
1467	4-Cl, 3-CH_3CH_2
1468	3-CH_3CH_2
1469	3-CH_3, 5-CH_3
1470	3-$(CH_3)_3C$
1471	4-F, 3-CH_3
1472	3-Cl, 4-Cl
1473	3,4-$(CH_2)_4$
1474	3-HCF_2CF_2O
1475	3-CHF_2O
1476	3-$(CH_3)_2N$
1477	3-cyclopropyl
1478	3-(2-furyl)
1479	3-CF_3CF_2
1480	4-NH_2
1481	3-CH_3, 4-CH_3, 5-CH_3
1482	4-$CH_3CH_2CH_2O$

Ex. No.	R_{SUB2}
1485	3-CF_3O-benzyloxy
1486	3-CF_3-benzyloxy
1487	3-F, 5-F-benzyloxy
1488	cyclohexylmethyleneoxy
1489	benzyloxy
1490	3-CF_3, 5-CF_3-benzyloxy
1491	4-CF_3O-benzyloxy
1492	4-CH_3CH_2-benzyloxy
1493	isopropoxy
1494	3-CF_3-benzyl
1495	isopropylthio
1496	cyclopentoxy
1497	3-Cl-5-pyridinyloxy
1498	3-CF_3S-benzyloxy
1499	3-CH_3, 4-CH_3-benzyloxy
1500	2-F, 3-CF_3-benzyloxy
1501	3-F, 5-CF_3-benzyloxy
1502	4-$(CH_3)_2CH$-benzyloxy
1503	1-phenylethoxy
1504	4-F, 3-CH_3-benzoyl
1505	3-CF_3-phenyl
1506	4-CH_3O-phenylamino

Ex. No.	R_{SUB1}
1483	3-CF_3
1484	2-NO_2

Ex. No.	R_{SUB2}
1507	cyclopropoxy
1508	4-NO_2-phenylthio

Example Table 7 (cont.). 3-[(*N*-aryl)[[haloalkyl]methyl]amino]-halo-2-propanols.



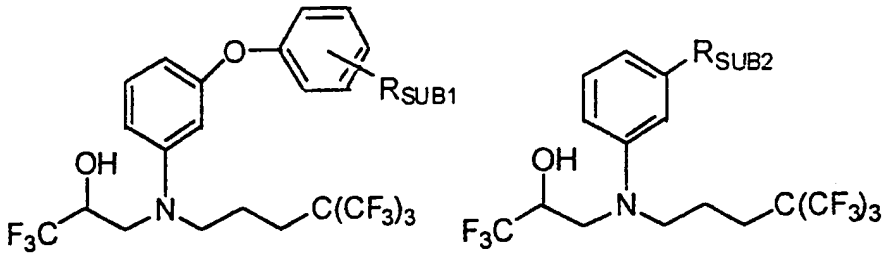
Ex. No.	R_{SUB1}
1509	3-isopropyl
1510	2-Cl, 3-Cl
1511	3-CF_3O
1512	4-F
1513	4-CH_3
1514	2-F, 5-Br
1515	4-Cl, 3-CH_3CH_2
1516	3-CH_3CH_2
1517	3-CH_3, 5-CH_3
1518	3-$(CH_3)_3C$
1519	4-F, 3-CH_3
1520	3-Cl, 4-Cl
1521	3,4-$(CH_2)_4$
1522	3-HCF_2CF_2O
1523	3-CHF_2O
1524	3-$(CH_3)_2N$
1525	3-cyclopropyl
1526	3-(2-furyl)

Ex. No.	R_{SUB2}
1533	3-CF_3O-benzyloxy
1534	3-CF_3-benzyloxy
1535	3-F, 5-F-benzyloxy
1536	cyclohexylmethyleneoxy
1537	benzyloxy
1538	3-CF_3, 5-CF_3-benzyloxy
1539	4-CF_3O-benzyloxy
1540	4-CH_3CH_2-benzyloxy
1541	isopropoxy
1542	3-CF_3-benzyl
1543	isopropylthio
1544	cyclopentoxy
1545	3-Cl-5-pyridinyloxy
1546	3-CF_3S-benzyloxy
1547	3-CH_3, 4-CH_3-benzyloxy
1548	2-F, 3-CF_3-benzyloxy
1549	3-F, 5-CF_3-benzyloxy
1550	4-$(CH_3)_2CH$-benzyloxy

Ex. No.	R_{SUB1}
1527	3-CF_3CF_2
1528	4-NH_2
1529	3-CH_3, 4-CH_3, 5-CH_3
1530	4-$CH_3CH_2CH_2O$
1531	3-CF_3
1532	2-NO_2

Ex. No.	R_{SUB2}
1551	1-phenylethoxy
1552	4-F, 3-CH_3-benzoyl
1553	3-CF_3-phenyl
1554	4-CH_3O-phenylamino
1555	cyclopropoxy
1556	4-NO_2-phenylthio

Example Table 7 (cont.). 3-[(*N*-aryl)[[haloalkyl]methyl]amino]-halo-2-propanols.



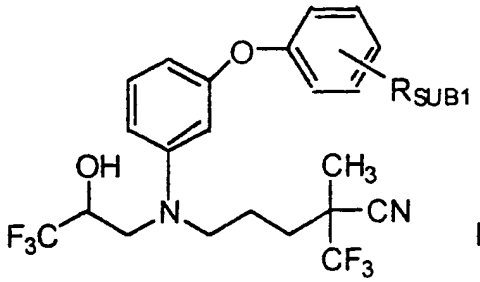
Ex. No.	R_{SUB1}
1557	3-isopropyl
1558	2-Cl, 3-Cl
1559	3-CF_3O
1560	4-F
1561	4-CH_3
1562	2-F, 5-Br
1563	4-Cl, 3-CH_3CH_2
1564	3-CH_3CH_2
1565	3-CH_3, 5-CH_3
1566	3-$(CH_3)_3C$
1567	4-F, 3-CH_3
1568	3-Cl, 4-Cl
1569	3,4-$(CH_2)_4$
1570	3-HCF_2CF_2O

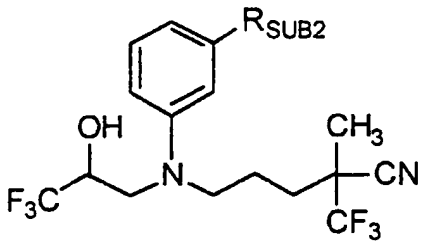
Ex. No.	R_{SUB2}
1581	3-CF_3O-benzyloxy
1582	3-CF_3-benzyloxy
1583	3-F, 5-F-benzyloxy
1584	cyclohexylmethyleneoxy
1585	benzyloxy
1586	3-CF_3, 5-CF_3-benzyloxy
1587	4-CF_3O-benzyloxy
1588	4-CH_3CH_2-benzyloxy
1589	isopropoxy
1590	3-CF_3-benzyl
1591	isopropylthio
1592	cyclopentoxy
1593	3-Cl-5-pyridinyloxy
1594	3-CF_3S-benzyloxy

Ex. No.	R_{SUB1}
1571	3-CHF_2O
1572	3-$(CH_3)_2N$
1573	3-cyclopropyl
1574	3-(2-furyl)
1575	3-CF_3CF_2
1576	4-NH_2
1577	3-CH_3, 4-CH_3, 5-CH_3
1578	4-$CH_3CH_2CH_2O$
1579	3-CF_3
1580	2-NO_2

Ex. No.	R_{SUB2}
1595	3-CH_3, 4-CH_3-benzyloxy
1596	2-F, 3-CF_3-benzyloxy
1597	3-F, 5-CF_3-benzyloxy
1598	4-$(CH_3)_2CH$-benzyloxy
1599	1-phenylethoxy
1600	4-F, 3-CH_3-benzoyl
1601	3-CF_3-phenyl
1602	4-CH_3O-phenylamino
1603	cyclopropoxy
1604	4-NO_2-phenylthio

Example Table 7 (cont.). 3-[(*N*-aryl)[[haloalkyl]methyl]amino]-halo-2-propanols.





Ex. No.	R_{SUB1}
1605	3-isopropyl
1606	2-Cl, 3-Cl
1607	3-CF_3O
1608	4-F
1609	4-CH_3
1610	2-F, 5-Br
1611	4-Cl, 3-CH_3CH_2
1612	3-CH_3CH_2
1613	3-CH_3, 5-CH_3

Ex. No.	R_{SUB2}
1629	3-CF_3O-benzyloxy
1630	3-CF_3-benzyloxy
1631	3-F, 5-F-benzyloxy
1632	cyclohexylmethyleneoxy
1633	benzyloxy
1634	3-CF_3, 5-CF_3-benzyloxy
1635	4-CF_3O-benzyloxy
1636	4-CH_3CH_2-benzyloxy
1637	isopropoxy

Ex. No.	R_{SUB1}
1614	3-$(CH_3)_3C$
1615	4-F, 3-CH_3
1616	3-Cl, 4-Cl
1617	3,4-$(CH_2)_4$
1618	3-HCF_2CF_2O
1619	3-CHF_2O
1620	3-$(CH_3)_2N$
1621	3-cyclopropyl
1622	3-(2-furyl)
1623	3-CF_3CF_2
1624	4-NH_2
1625	3-CH_3, 4-CH_3, 5-CH_3
1626	4-$CH_3CH_2CH_2O$
1627	3-CF_3
1628	2-NO_2

Ex. No.	R_{SUB2}
1638	3-CF_3-benzyl
1639	isopropylthio
1640	cyclopentoxy
1641	3-Cl-5-pyridinyloxy
1642	3-CF_3S-benzyloxy
1643	3-CH_3, 4-CH_3-benzyloxy
1644	2-F, 3-CF_3-benzyloxy
1645	3-F, 5-CF_3-benzyloxy
1646	4-$(CH_3)_2CH$-benzyloxy
1647	1-phenylethoxy
1648	4-F, 3-CH_3-benzoyl
1649	3-CF_3-phenyl
1650	4-CH_3O-phenylamino
1651	cyclopropoxy
1652	4-NO_2-phenylthio

BIOASSAYS

CETP Activity *In Vitro*

ASSAY OF CETP INHIBITION USING PURIFIED COMPONENTS (RECONSTITUTED BUFFER ASSAY)

The ability of compounds to inhibit CETP activity was assessed using an *in vitro* assay that measured the rate of transfer of radiolabeled cholesteryl ester ([^{3}H]CE) from HDL donor particles to LDL acceptor particles. Details of the assay are provided by Glenn, K. C. et al. (Glenn and Melton, "Quantification of Cholesteryl Ester Transfer Protein (CETP): A) CETP Activity and B) Immunochemical Assay of CETP Protein," *Meth. Enzymol.*, 263, 339-351 (1996)). Human recombinant CETP can be obtained from the serum-free conditioned medium of CHO cells transfected with a cDNA for CETP and purified as described by Wang, S. et al. (*J. Biol. Chem. 267*, 17487-17490 (1992)). To measure CETP activity, [^{3}H]CE-labeled-HDL, LDL, CETP and assay buffer (50 mM tris(hydroxymethyl)aminomethane, pH 7.4; 150 mM sodium chloride; 2 mM ethylenediamine-tetraacetic acid (EDTA); 1% bovine serum albumin) were incubated in a final volume of 200 μL, for 2 hours at 37 °C in 96 well plates. Inhibitors were included in the assay by diluting from a 10 mM DMSO stock solution into 16% (v/v) aqueous DMSO so that the final concentration of inhibitor was 800 μM. The inhibitors were then diluted 1:1 with CETP in assay buffer, and then 25 μL of that solution was mixed with 175 μL of lipoprotein pool for assay. Following incubation, LDL was differentially precipitated by the addition of 50 μL of 1% (w/v) dextran sulfate/0.5 M magnesium chloride, mixed by vortex, and incubated at room temperature for 10 minutes. A potion of the solution (200 μL) was transferred to a filter plate (Millipore). After filtration, the radioactivity present in the precipitated LDL was measured by liquid scintillation counting. Correction for non-specific transfer or precipitation was made by including samples that do not contain CETP. The rate of [^{3}H]CE transfer using this assay was linear with respect to time and CETP concentration, up to 25-30% of [^{3}H]CE transferred.

The potency of test compounds was determined by performing the above described assay in the presence of varying concentrations of the test compounds and determining the concentration required for 50% inhibition of transfer of [^{3}H]CE from HDL to LDL. This value was defined as the IC_{50}. The IC_{50}

values determined from this assay are accurate when the IC_{50} is greater than 10 nM. In the case where compounds have greater inhibitory potency, accurate measurements of IC_{50} may be determined using longer incubation times (up to 18 hours) and lower final concentrations of CETP (< 50 nM).

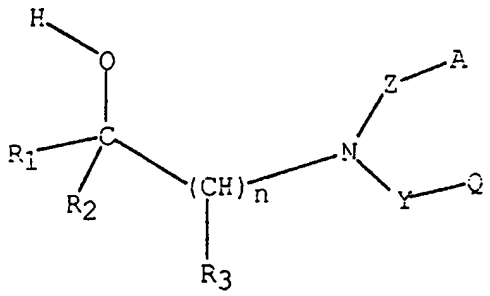
Examples of IC_{50} values determined by these methods are summarized in Table 3.

Table 3. Inhibition of CETP Activity by Examples in Reconstituted Buffer Assay.

Ex. No.	IC_{50} (μM)
18	11
1	15
16	15
9	18
4	20
11	45
8	45
10	50
14	55
12	60
17	60
13	80
7	100
2	100
6	>100.0
5	>100.0
15	>100.0
3	not tested

What we claim is:

1. The compound having the formula of:

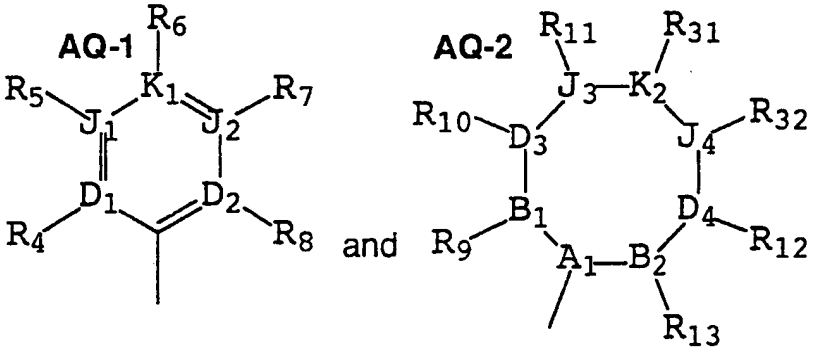


or a pharmaceutically acceptable salt thereof, wherein;

n is an integer selected from 1 through 2;

A and Q are independently selected from the group consisting of

$-CH_2(CR_{37}R_{38})_v-(CR_{33}R_{34})_u-T-(CR_{35}R_{36})_w-H$,



with the provisos that one of A and Q must be AQ-1 and that one of A and Q must be selected from the group consisting of AQ-2 and

$-CH_2(CR_{37}R_{38})_v-(CR_{33}R_{34})_u-T-(CR_{35}R_{36})_w-H$;

T is selected from the group consisting of a single covalent bond, O, S, $S(O)$, $S(O)_2$, $C(R_{33})=C(R_{35})$, and C≡C;

v is an integer selected from 0 through 1 with the proviso that v is 1 when any one of R_{33}, R_{34}, R_{35}, and R_{36} is aryl or heteroaryl;

u and w are integers independently selected from 0 through 6;

A_1 is $C(R_{30})$;

D_1, D_2, J_1, J_2 and K_1 are independently selected from the group consisting of C, N, O, S and a covalent bond with the provisos that no more than one of D_1, D_2, J_1, J_2 and K_1 is a covalent bond, no more than one of D_1, D_2, J_1, J_2 and K_1 is O, no more than one of D_1, D_2, J_1, J_2 and K_1 is S, one of D_1, D_2, J_1, J_2 and K_1 must be a covalent bond when two of D_1, D_2, J_1, J_2 and K_1 are O and S, and no more than four of D_1, D_2, J_1, J_2 and K_1 are N;

B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are independently selected from the group consisting of C, $C(R_{30})$, N, O, S and a covalent bond with the provisos that no more than 5 of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are a covalent bond, no more than two of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are O, no more than two of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are S, no more than two of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are simultaneously O and S, and no more than two of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are N;

B_1 and D_3, D_3 and J_3, J_3 and K_2, K_2 and J_4, J_4 and D_4, and D_4 and B_2 are independently selected to form an in-ring spacer pair wherein said spacer pair is selected from the group consisting of $C(R_{33})=C(R_{35})$ and N=N with the provisos that AQ-2 must be a ring of at least five contiguous members, that no more than two of the group of said spacer pairs are simultaneously $C(R_{33})=C(R_{35})$, and that no more than one of the group of said spacer pairs is N=N unless the other spacer pairs are other than $C(R_{33})=C(R_{35})$, O, N, and S;

R_1 is selected from the group consisting of haloalkyl and haloalkoxymethyl;

R_2 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, haloalkoxy, haloalkoxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, and heteroaryl;

R_3 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, and haloalkoxyalkyl;

Y is selected from the group consisting of a covalent single bond, $(CH_2)_q$ wherein q is an integer selected from 1 through 2, and $(CH_2)_j$-O-$(CH_2)_k$ wherein j and k are integers independently selected from 0 through 1;

Z is selected from the group consisting of covalent single bond, $(CH_2)_q$ wherein q is an integer selected from 1 through 2, and $(CH_2)_j$-O-$(CH_2)_k$ wherein j and k are integers independently selected from 0 through 1;

R_4, R_8, R_9, and R_{13} are independently selected from the group consisting of hydrido, halo, haloalkyl, and alkyl ;

R_{30} is selected from the group consisting of hydrido, alkoxy, alkoxyalkyl, halo, haloalkyl, alkylamino, alkylthio, alkylthioalkyl, alkyl, alkenyl, haloalkoxy, and haloalkoxyalkyl with the proviso that R_{30} is selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen;

R_{30}, when bonded to A_1, is taken together to form an intra-ring linear spacer connecting the A_1-carbon at the point of attachment of R_{30} to the point of bonding of a group selected from the group consisting of R_{10}, R_{11}, R_{12}, R_{31}, and R_{32} wherein said intra-ring linear spacer is selected from the group consisting of a covalent single bond and a spacer moiety having from 1 through 6 contiguous atoms to form a ring selected from the group consisting of a

cycloalkyl having from 3 through 10 contiguous members, a cycloalkenyl having from 5 through 10 contiguous members, and a heterocyclyl having from 5 through 10 contiguous members;

R_{30}, when bonded to A_1, is taken together to form an intra-ring branched spacer connecting the A_1-carbon at the point of attachment of R_{30} to the points of bonding of each member of any one of substituent pairs selected from the group consisting of subsitituent pairs R_{10} and R_{11}, R_{10} and R_{31}, R_{10} and R_{32}, R_{10} and R_{12}, R_{11} and R_{31}, R_{11} and R_{32}, R_{11} and R_{12}, R_{31} and R_{32}, R_{31} and R_{12}, and R_{32} and R_{12} and wherein said intra-ring branched spacer is selected to form two rings selected from the group consisting of cycloalkyl having from 3 through 10 contiguous members, cycloalkenyl having from 5 through 10 contiguous members, and heterocyclyl having from 5 through 10 contiguous members;

R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, R_{32} , R_{33}, R_{34}, R_{35}, and R_{36} are independently selected from the group consisting of hydrido, carboxy, heteroaralkylthio, heteroaralkoxy, cycloalkylamino, acylalkyl, acylalkoxy, aroylalkoxy, heterocyclyloxy, aralkylaryl, aralkyl, aralkenyl, aralkynyl, heterocyclyl, perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, aralkylsulfinyl, aralkylsulfinylalkyl, halocycloalkyl, halocycloalkenyl, cycloalkylsulfinyl, cycloalkylsulfinylalkyl, cycloalkylsulfonyl, cycloalkylsulfonylalkyl, heteroarylamino, N-heteroarylamino-N-alkylamino, heteroarylaminoalkyl,haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, haloalkoxylalkyl, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, cycloalkoxyalkyl, cycloalkylalkoxy, cycloalkenyloxyalkyl, cycloalkylenedioxy, halocycloalkoxy, halocycloalkoxyalkyl, halocycloalkenyloxy, halocycloalkenyloxyalkyl, hydroxy, amino, thio, nitro, lower alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylthioalkyl, heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, arylsulfonylalkyl, heteroarylsulfinylalkyl, heteroarylsulfonylalkyl, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfinylalkyl, haloalkylsulfonylalkyl.

alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, monoarylamidosulfonyl, arylsulfonamido, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, heterocyclylsulfonyl, heterocyclylthio, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, alkenyloxy, alkenyloxyalky, alkylenedioxy, haloalkylenedioxy, cycloalkyl, cycloalkylalkanoyl, cycloalkenyl, lower cycloalkylalkyl, lower cycloalkenylalkyl, halo, haloalkyl, haloalkenyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydoxyheteroaralkyl, haloalkoxyalkyl, aryl, heteroaralkynyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, arylalkenyl, heteroarylalkenyl, carboxyalkyl, carboalkoxy, alkoxycarboxamido, alkylamidocarbonylamido, arylamidocarbonylamido, carboalkoxyalkyl, carboalkoxyalkenyl, carboaralkoxy, carboxamido, carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl with the provisos that R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, R_{32}, R_{33}, R_{34}, R_{35}, and R_{36} are each independently selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen, that no more than three of the R_{33} and R_{34} substituents are simultaneously selected from other than the group consisting of of hydrido and halo, and that no more than three of the R_{35} and R_{36} substituents are simultaneously selected from other than the group consistubg of hydrido and halo;

R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, and R_{32} are independently selected to be oxo with the provisos that B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are independently selected from the group consisting of C and S, no more than two of R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, and R_{32} are simultaneously oxo, and that R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, and R_{32} are each independently selected to

maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen;

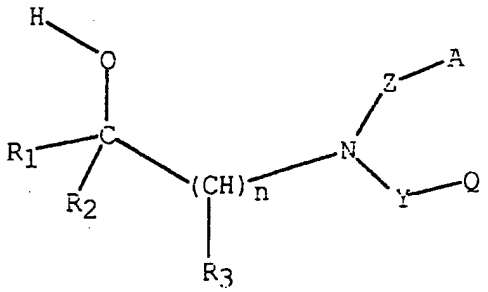
R_4 and R_5, R_5 and R_6, R_6 and R_7, R_7 and R_8, R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{31}, R_{31} and R_{32}, R_{32} and R_{12}, and R_{12} and R_{13} are independently selected to form spacer pairs wherein a spacer pair is taken together to form a linear moiety having from 3 through 6 contiguous atoms connecting the points of bonding of said spacer pair members to form a ring selected from the group consisting of a cycloalkenyl ring having 5 through 8 contiguous members, a partially saturated heterocyclyl ring having 5 through 8 contiguous members, a heteroaryl ring having 5 through 6 contiguous members, and an aryl with the provisos that no more than one of the group consisting of spacer pairs R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8, is used at the same time and that no more than one of the group consisting of spacer pairs R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{31}, R_{31} and R_{32}, R_{32} and R_{12}, and R_{12} and R_{13} is used at the same time;

R_9 and R_{11}, R_9 and R_{12}, R_9 and R_{13}, R_9 and R_{31}, R_9 and R_{32}, R_{10} and R_{12}, R_{10} and R_{13}, R_{10} and R_{31}, R_{10} and R_{32}, R_{11} and R_{12}, R_{11} and R_{13}, R_{11} and R_{32}, R_{12} and R_{31}, R_{13} and R_{31}, and R_{13} and R_{32} are independently selected to form a spacer pair wherein said spacer pair is taken together to form a linear spacer moiety selected from the group consisting of a covalent single bond and a moiety having from 1 through 3 contiguous atoms to form a ring selected from the group consisting of a cycloalkyl having from 3 through 8 contiguous members, a cycloalkenyl having from 5 through 8 contiguous members, a saturated heterocyclyl having from 5 through 8 contiguous members and a partially saturated heterocyclyl having from 5 through 8 contiguous members with the provisos that no more than one of said group of spacer pairs is used at the same time;

R_{37} and R_{38} are independently selected from the group consisting of hydrido, alkoxy, alkoxyalkyl, hydroxy, amino, thio, halo, haloalkyl,

alkylamino, alkylthio, alkylthioalkyl, cyano, alkyl, alkenyl, haloalkoxy, and haloalkoxyalkyl.

2. The compound as recited in Claim 1 having the formula of:

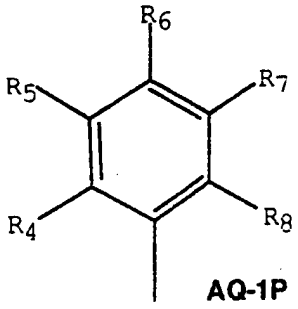


or a pharmaceutically acceptable salt thereof, wherein;

n is an integer selected from 1 through 2;

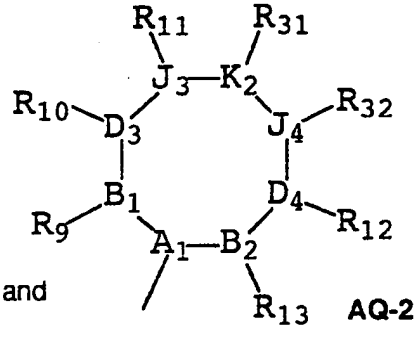
A and Q are independently selected from the group consisting of

$-CH_2(CR_{37}R_{38})_v-(CR_{33}R_{34})_u-T-(CR_{35}R_{36})_w-H$,



AQ-1P

, and



AQ-2,

with the provisos that one of A and Q must be AQ-1P and that one of A and Q must be selected from the group consisting of AQ-2 and

$-CH_2(CR_{37}R_{38})_v-(CR_{33}R_{34})_u-T-(CR_{35}R_{36})_w-H$;

T is selected from the group consisting of a single covalent bond, O, S, S(O), $S(O)_2$, $C(R_{33})=C(R_{35})$, and C≡C;

v is an integer selected from 0 through 1 with the proviso that v is 1 when any one of R_{33}, R_{34}, R_{35}, and R_{36} is aryl or heteroaryl;

u and w are integers independently selected from 0 through 6;

A_1 is $C(R_{30})$;

B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are independently selected from the group consisting of C, $C(R_{30})$, N, O, S and a covalent bond with the provisos that no more than 5 of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are a covalent bond, no more than two of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are O, no more than two of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are S, no more than two of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are simultaneously O and S, and no more than two of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are N;

B_1 and D_3, D_3 and J_3, J_3 and K_2, K_2 and J_4, J_4 and D_4, and D_4 and B_2 are independently selected to form an in-ring spacer pair wherein said spacer pair is selected from the group consisting of $C(R_{33})=C(R_{35})$ and N=N with the provisos that AQ-2 must be a ring of at least five contiguous members, that no more than two of the group of said spacer pairs are simultaneously $C(R_{33})=C(R_{35})$, and that no more than one of the group of said spacer pairs is N=N unless the other spacer pairs are other than $C(R_{33})=C(R_{35})$, O, N, and S;

R_1 is selected from the group consisting of haloalkyl and haloalkoxymethyl;

R_2 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, haloalkoxy, haloalkoxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, and heteroaryl;

R_3 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, and haloalkoxyalkyl;

Y is selected from the group consisting of a covalent single bond, $(CH_2)_q$ wherein q is an integer selected from 1 through 2, and $(CH_2)_j$-O-$(CH_2)_k$ wherein j and k are integers independently selected from 0 through 1;

Z is selected from the group consisting of covalent single bond, $(CH_2)_q$ wherein q is an integer selected from 1 through 2, and $(CH_2)_j$-O-$(CH_2)_k$ wherein j and k are integers independently selected from 0 through 1;

R_{30} is selected from the group consisting of hydrido, alkoxy, alkoxyalkyl, halo, haloalkyl, alkylamino, alkylthio, alkylthioalkyl, alkyl, alkenyl, haloalkoxy, and haloalkoxyalkyl with the proviso that R_{30} is selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen;

R_{30}, when bonded to A_1, is taken together to form an intra-ring linear spacer connecting the A_1-carbon at the point of attachment of R_{30} to the point of bonding of a group selected from the group consisting of R_{10}, R_{11}, R_{12}, R_{31}, and R_{32} wherein said intra-ring linear spacer is selected from the group consisting of a covalent single bond and a spacer moiety having from 1 through 6 contiguous atoms to form a ring selected from the group consisting of a cycloalkyl having from 3 through 10 contiguous members, a cycloalkenyl having from 5 through 10 contiguous members, and a heterocyclyl having from 5 through 10 contiguous members;

R_{30}, when bonded to A_1, is taken together to form an intra-ring branched spacer connecting the A_1-carbon at the point of attachment of R_{30} to the points of bonding of each member of any one of substituent pairs selected from the group consisting of subsitituent pairs R_{10} and R_{11}, R_{10} and R_{31}, R_{10} and R_{32}, R_{10} and R_{12}, R_{11} and R_{31}, R_{11} and R_{32}, R_{11} and R_{12}, R_{31}

and R_{32}, R_{31} and R_{12}, and R_{32} and R_{12} and wherein said intra-ring branched spacer is selected to form two rings selected from the group consisting of cycloalkyl having from 3 through 10 contiguous members, cycloalkenyl having from 5 through 10 contiguous members, and heterocyclyl having from 5 through 10 contiguous members;

R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, R_{32}, R_{33},

R_{34}, R_{35}, and R_{36} are independently selected from the group consisting of hydrido, carboxy, heteroaralkylthio, heteroaralkoxy, cycloalkylamino, acylalkyl, acylalkoxy, aroylalkoxy, heterocyclyloxy, aralkylaryl, aralkyl, aralkenyl, aralkynyl, heterocyclyl, perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, aralkylsulfinyl, aralkylsulfinylalkyl, halocycloalkyl, halocycloalkenyl, cycloalkylsulfinyl, cycloalkylsulfinylalkyl, cycloalkylsulfonyl, cycloalkylsulfonylalkyl, heteroarylamino, N-heteroarylamino-N-alkylamino, heteroarylaminoalkyl,haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, haloalkoxylalkyl, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, cycloalkoxyalkyl, cycloalkylalkoxy, cycloalkenyloxyalkyl, cycloalkylenedioxy, halocycloalkoxy, halocycloalkoxyalkyl, halocycloalkenyloxy, halocycloalkenyloxyalkyl, hydroxy, amino, thio, nitro, lower alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylthioalkyl, heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, arylsulfonylalkyl, heteroarylsulfinylalkyl, heteroarylsulfonylalkyl, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfinylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, monoarylamidosulfonyl, arylsulfonamido, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, heterocyclylsulfonyl, heterocyclylthio, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, alkenyloxy, alkenyloxyalky, alkylenedioxy, haloalkylenedioxy, cycloalkyl, cycloalkylalkanoyl, cycloalkenyl, lower cycloalkylalkyl, lower cycloalkenylalkyl, halo, haloalkyl, haloalkenyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydoxyheteroaralkyl, haloalkoxyalkyl, aryl,

heteroaralkynyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, arylalkenyl, heteroarylalkenyl, carboxyalkyl, carboalkoxy, alkoxycarboxamido, alkylamidocarbonylamido, arylamidocarbonylamido, carboalkoxyalkyl, carboalkoxyalkenyl, carboaralkoxy, carboxamido, carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl with the provisos that R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, R_{32}, R_{33}, R_{34}, R_{35}, and R_{36} are each independently selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen, that no more than three of the R_{33} and R_{34} substituents are simultaneously selected from other than the group consisting of of hydrido and halo, and that no more than three of the R_{35} and R_{36} substituents are simultaneously selected from other than the group consistubg of hydrido and halo;

R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, and R_{32} are independently selected to be oxo with the provisos that B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are independently selected from the group consisting of C and S, no more than two of R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, and R_{32} are simultaneously oxo, and that R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, and R_{32} are each independently selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen;

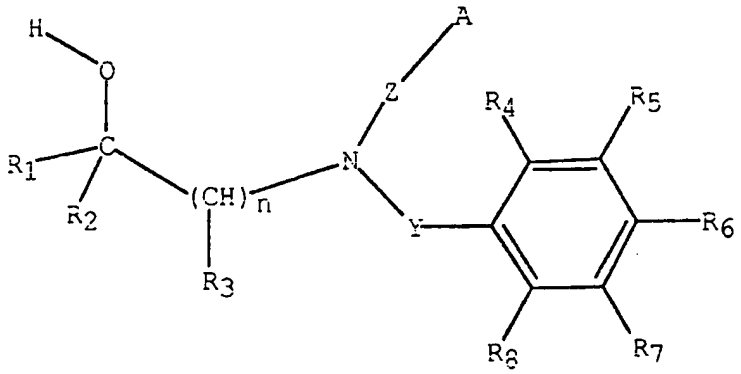
R_4 and R_5, R_5 and R_6, R_6 and R_7, R_7 and R_8, R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{31}, R_{31} and R_{32}, R_{32} and R_{12}, and R_{12} and R_{13} are independently selected to form spacer pairs wherein a spacer pair is taken together to form a linear moiety having from 3 through 6 contiguous atoms connecting the points of bonding of said spacer pair members to form a ring selected from the group consisting of a cycloalkenyl ring having 5 through 8

contiguous members, a partially saturated heterocyclyl ring having 5 through 8 contiguous members, a heteroaryl ring having 5 through 6 contiguous members, and an aryl with the provisos that no more than one of the group consisting of spacer pairs R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8, is used at the same time and that no more than one of the group consisting of spacer pairs R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{31}, R_{31} and R_{32}, R_{32} and R_{12}, and R_{12} and R_{13} is used at the same time;

R_9 and R_{11}, R_9 and R_{12}, R_9 and R_{13}, R_9 and R_{31}, R_9 and R_{32}, R_{10} and R_{12}, R_{10} and R_{13}, R_{10} and R_{31}, R_{10} and R_{32}, R_{11} and R_{12}, R_{11} and R_{13}, R_{11} and R_{32}, R_{12} and R_{31}, R_{13} and R_{31}, and R_{13} and R_{32} are independently selected to form a spacer pair wherein said spacer pair is taken together to form a linear spacer moiety selected from the group consisting of a covalent single bond and a moiety having from 1 through 3 contiguous atoms to form a ring selected from the group consisting of a cycloalkyl having from 3 through 8 contiguous members, a cycloalkenyl having from 5 through 8 contiguous members, a saturated heterocyclyl having from 5 through 8 contiguous members and a partially saturated heterocyclyl having from 5 through 8 contiguous members with the provisos that no more than one of said group of spacer pairs is used at the same time;

R_{37} and R_{38} are independently selected from the group consisting of hydrido, alkoxy, alkoxyalkyl, hydroxy, amino, thio, halo, haloalkyl, alkylamino, alkylthio, alkylthioalkyl, cyano, alkyl, alkenyl, haloalkoxy, and haloalkoxyalkyl.

3. The compound as recited in Claim 2 having the formula of:



or a pharmaceutically acceptable salt thereof, wherein;

n is an integer selected from 1 through 2;

A is selected from the group consisting of C3-C10 cycloalkyl, C5-C10 cycloalkenyl, C4-C9 saturated heterocyclyl, and C4-C9 partially saturated heterocyclyl, wherein each ring carbon may be optionally substituted with R_{30}, a ring carbon other than the ring carbon at the point of attachment of A to Z may be optionally substituted with oxo provided that no more than one ring carbon is substituted by oxo at the same time, ring carbon and nitrogen atoms adjacent to the carbon atom at the point of attachment may be optionally substituted with R_9 or R_{13}, a ring carbon or nitrogen atom adjacent to the R_9 position and two atoms from the point of attachment may be substituted with R_{10}, a ring carbon or nitrogen atom adjacent to the R_{13} position and two atoms from the point of attachment may be substituted with R_{12}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{10} position may be substituted with R_{11}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{12} position may be substituted with R_{32}, and a ring carbon or nitrogen atom four atoms from

the point of attachment and adjacent to the R_{11} and R_{32} positions may be substituted with R_{31};

R_1 is selected from the group consisting of haloalkyl and haloalkoxymethyl;

R_2 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, haloalkoxy, haloalkoxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, and heteroaryl;

R_3 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, and haloalkoxyalkyl;

Y and Z are independently selected from the group consisting of a covalent single bond, oxy and alkylene;

R_4 and R_8 are independently selected from the group consisting of hydrido and halo;

R_9 and R_{13} are halo;

R_5, R_6, and R_7 are independently selected from the group consisting of hydrido, alkyl, halo, haloalkyl, haloalkoxy, aryl, alkylthio, arylamino, arylthio, aroyl, arylsulfonyl, aryloxy, aralkoxy, heteroaryloxy, alkoxy, aralkyl, cycloalkoxy, cycloalkylalkoxy, cycloalkylalkanoyl, heteroaryl, cycloalkyl, haloalkylthio, hydroxyhaloalkyl, heteroaralkoxy, heterocyclyloxy, aralkylaryl, heteroaryloxyalkyl, heteroarylthio, and heteroarylsulfonyl;

R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8 are independently selected to form spacer pairs wherein a spacer pair is taken together to form a linear moiety having from 3 through 6 contiguous atoms connecting the points of bonding of said spacer pair members to form a ring selected from the group consisting of a cycloalkenyl ring having 5 through 8 contiguous members, a partially saturated heterocyclyl ring having 5 through 8 contiguous members, a heteroaryl ring having 5 through 6 contiguous members, and an aryl with the

proviso that no more than one of the group consisting of spacer pairs R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8, is used at the same time;

R_{10}, R_{11}, R_{12}, R_{31}, and R_{32} are independently selected from the group group consisting of alkyl, halo, haloalkyl, haloalkoxy, aryl, alkylthio, arylamino, arylthio, aroyl, arylsulfonyl, aryloxy, aralkoxy, heteroaryloxy, alkoxy, aralkyl, cycloalkoxy, cycloalkylalkoxy, cycloalkylalkanoyl, heteroaryl, cycloalkyl, haloalkylthio, hydroxyhaloalkyl, heteroaralkoxy, heterocyclyloxy, aralkylaryl, heteroaryloxyalkyl, heteroarylthio, and heteroarylsulfonyl;

R_{30} is selected from the group consisting of alkoxy, alkoxyalkyl, halo, haloalkyl, alkylamino, alkylthio, alkylthioalkyl, alkyl, alkenyl, haloalkoxy, and haloalkoxyalkyl.

4. The compound as recited in Claim 3 or a pharmaceutically acceptable salt thereof, wherein;

n is the integer 1;

A is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclopent-2-enyl, cyclopent-3-enyl, cyclohexyl, 4-methylcyclohexyl, 4-chloro-3-ethylphenoxycyclohexyl, 3-trifluoromethoxyphenoxycyclohexyl, 3-trifluoromethylcyclohexyl, 4-trifluoromethylcyclohexyl, 3,5-bis-trifluoromethylcyclohexyl, adamantyl, 3-trifluoromethyladamantyl, norbornyl, 3-trifluoromethylnorbornyl, norbornenyl, 7-oxabicyclo[2.2.1]heptan-2-yl, bicyclo[3.1.0]hexan-6-yl, cyclohex-2-enyl, cyclohex-3-enyl, cycloheptyl, cyclohept-2-enyl, cyclohept-3-enyl, cyclooctyl, cyclooct-2-enyl, cyclooct-3-enyl, cyclooct-4-enyl, 2-morpholinyl, 3-morpholinyl, 4-morpholinyl, 1-piperazinyl, 2-piperazinyl, 1-piperidinyl, 2-piperidinyl, 3-piperidinyl, 4-piperidinyl, 1-pyrrolidinyl, 2-pyrrolidinyl, 3-pyrrolidinyl, 2-dioxanyl, 2H-2-pyranyl, 2H-3-pyranyl, 2H-4-pyranyl, 4H-2-pyranyl, 4H-3-pyranyl, 4H-4-pyranyl, 2H-pyran-2-one-3-yl, 2H-pyran-2-one-4-yl, 2H-pyran-2-one-5-yl, 4H-pyran-4-one-2-yl, 4H-pyran-4-one-3-yl, 2-tetrahydrofuranyl, 3-tetrahydrofuranyl, 2-tetrahydropyranyl, 3-tetrahydropyranyl, 4-tetrahydropyranyl, 2-tetrahydrothienyl, and 3-

tetrahydrothienyl, wherein each ring carbon may be optionally substituted with R_{30}, a ring carbon other than the ring carbon at the point of attachment of A to Z may be optionally substituted with oxo provided that no more than one ring carbon is substituted by oxo at the same time, ring carbon and nitrogen atoms adjacent to the carbon atom at the point of attachment may be optionally substituted with R_9 or R_{13}, a ring carbon or nitrogen atom adjacent to the R_9 position and two atoms from the point of attachment may be substituted with R_{10}, a ring carbon or nitrogen atom adjacent to the R_{13} position and two atoms from the point of attachment may be substituted with R_{12}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{10} position may be substituted with R_{11}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{12} position may be substituted with R_{32}, and a ring carbon or nitrogen atom four atoms from the point of attachment and adjacent to the R_{11} and R_{32} positions may be substituted with R_{31};

R_1 is selected from the group consisting of trifluoromethyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, difluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

R_2 is selected from the group consisting of hydrido, methyl, ethyl, propyl, butyl, vinyl, phenyl, 4-trifluoromethylphenyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, difluoromethyl, pentafluoroethyl, trifluoromethyl, and 2,2,3,3,3-pentafluoropropyl;

R_3 is selected from the group consisting of hydrido, phenyl, 4-trifluoromethylphenyl, methyl, ethyl, vinyl, trifluoromethyl, trifluoromethoxymethyl, difluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

Y and Z are independently selected from the group consisting of a covalent single bond, oxy, and methylene with the proviso that only one of Y and Z are simultaneously oxy;

R_4 and R_8 are independently selected from the group consisting of hydrido and fluoro;

R_9 and R_{13} are fluoro;

R_5, R_{10} and R_{12} are independently selected from the group consisting of 4-aminophenoxy, benzoyl, benzyl, benzyloxy, 5-bromo-2-fluorophenoxy, 4-bromo-3-fluorophenoxy, 4-bromo-2-nitrophenoxy, 3-bromobenzyloxy, 4-bromobenzyloxy, 4-bromophenoxy, 5-bromopyrid-2-yloxy, 4-butoxyphenoxy, chloro, 3-chlorobenzyl, 2-chlorophenoxy, 4-chlorophenoxy, 4-chloro-3-ethylphenoxy, 3-chloro-4-fluorobenzyl, 3-chloro-4-fluorophenyl, 3-chloro-2-fluorobenzyloxy, 3-chlorobenzyloxy, 4-chlorobenzyloxy, 4-chloro-3-methylphenoxy, 2-chloro-4-fluorophenoxy, 4-chloro-2-fluorophenoxy, 4-chlorophenoxy, 3-chloro-4-ethylphenoxy, 3-chloro-4-methylphenoxy, 3-chloro-4-fluorophenoxy, 4-chloro-3-fluorophenoxy, 4-chlorophenylamino, 5-chloropyrid-3-yloxy, 2-cyanopyrid-3-yloxy, 4-cyanophenoxy, cyclobutoxy, cyclobutyl, cyclohexoxy, cyclohexylmethoxy, cyclopentoxy, cyclopentyl, cyclopentylcarbonyl, cyclopropyl, cyclopropylmethoxy, cyclopropoxy, 2,3-dichlorophenoxy, 2,4-dichlorophenoxy, 2,4-dichlorophenyl, 3,5-dichlorophenyl, 3,5-dichlorobenzyl, 3,4-dichlorophenoxy, 3,4-difluorophenoxy, 2,3-difluorobenzyloxy, 2,4-difluorobenzyloxy, 3,4-difluorobenzyloxy, 2,5-difluorobenzyloxy, 3,5-difluorophenoxy, 3,4-difluorophenyl, 3,5-difluorobenzyloxy, 4-difluoromethoxybenzyloxy, 2,3-difluorophenoxy, 2,4-difluorophenoxy, 2,5-difluorophenoxy, 3,5-dimethoxyphenoxy, 3-dimethylaminophenoxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 3,4-dimethylbenzyl, 3,4-dimethylbenzyloxy, 3,5-dimethylbenzyloxy, 2,2-dimethylpropoxy, 1,3-dioxan-2-yl, 1,4-dioxan-2-yl, 1,3-dioxolan-2-yl, ethoxy, 4-ethoxyphenoxy, 4-ethylbenzyloxy, 3-ethylphenoxy, 4-ethylaminophenoxy, 3-ethyl-5-methylphenoxy, fluoro, 4-fluoro-3-methylbenzyl, 4-fluoro-3-methylphenyl, 4-fluoro-3-methylbenzoyl, 4-fluorobenzyloxy,

2-fluoro-3-methylphenoxy, 3-fluoro-4-methylphenoxy, 3-fluorophenoxy, 3-fluoro-2-nitrophenoxy, 2-fluoro-3-trifluoromethylbenzyloxy, 3-fluoro-5-trifluoromethylbenzyloxy, 4-fluoro-2-trifluoromethylbenzyloxy, 4-fluoro-3-trifluoromethylbenzyloxy, 2-fluorophenoxy, 4-fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2-fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4-trifluoromethylphenoxy, 4-fluoropyrid-2-yloxy, 2-furyl, 3-furyl, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, 2-hydroxy-3,3,3-trifluoropropoxy, 3-iodobenzyloxy, isobutyl, isobutylamino, isobutoxy, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, isopropoxy, isopropyl, 4-isopropylbenzyloxy, 3-isopropylphenoxy, 4-isopropylphenoxy, isopropylthio, 4-isopropyl-3-methylphenoxy, 3-isothiazolyl, 4-isothiazolyl, 5-isothiazolyl, 3-methoxybenzyl, 4-methoxycarbonylbutoxy, 3-methoxycarbonylprop-2-enyloxy, 4-methoxyphenyl, 3-methoxyphenylamino, 4-methoxyphenylamino, 3-methylbenzyloxy, 4-methylbenzyloxy, 3-methylphenoxy, 3-methyl-4-methylthiophenoxy, 4-methylphenoxy, 1-methylpropoxy, 2-methylpyrid-5-yloxy, 4-methylthiophenoxy, 2-naphthyloxy, 2-nitrophenoxy, 4-nitrophenoxy, 3-nitrophenyl, 4-nitrophenylthio, 2-oxazolyl, 4-oxazolyl, 5-oxazolyl, pentafluoroethyl, pentafluoroethylthio, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, phenoxy, phenylamino, 1-phenylethoxy, phenylsulfonyl, 4-propanoylphenoxy, propoxy, 4-propylphenoxy, 4-propoxyphenoxy, thiophen-3-yl, *sec*-butyl, 4-*sec*-butylphenoxy,*tert*-butoxy, 3-*tert*-butylphenoxy, 4-*tert*-butylphenoxy, 1,1,2,2-tetrafluoroethoxy, tetrahydrofuran-2-yl, 2-(5,6,7,8-tetrahydronaphthyloxy), thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, thiophen-2-yl, 2,3,5-trifluorobenzyloxy, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, 3,3,3-trifluoro-2-hydroxypropyl, trifluoromethoxy, 3-trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, 3-trifluoromethoxyphenoxy, 4-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 4-trifluoromethylbenzyloxy, 2,4-bis-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, 3-trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3-trifluoromethylphenyl, 3-trifluoromethylthiobenzyloxy, 4-trifluoromethylthiobenzyloxy, 2,3,4-trifluorophenoxy,

2,3,4-trifluorophenyl, 2,3,5-trifluorophenoxy, 3,4,5-trimethylphenoxy, 3-difluoromethoxyphenoxy, 3-pentafluoroethylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 3-trifluoromethylthiophenoxy, and trifluoromethylthio;

R_6, R_{11}, R_{31}, and R_{32} are independently selected from the group consisting of chloro, fluoro, hydrido, pentafluoroethyl, 1,1,2,2-tetrafluoroethoxy, trifluoromethyl, and trifluoromethoxy;

R_7 is selected from the group consisting of hydrido, fluoro, and trifluoromethyl;

R_{30} is selected from the group consisting of chloro, ethoxy, ethyl, fluoro, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, isobutyl, isobutoxy, isopropoxy, isopropyl, isopropylthio, methyl pentafluoroethyl, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, propoxy, propyl, *sec*-butyl, *tert*-butoxy, 1,1,2,2-tetrafluoroethoxy, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, trifluoromethoxy, and trifluoromethyl.

5. The compound as recited in Claim 4 or a pharmaceutically acceptable salt thereof, wherein;

n is the integer 1;

A is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 4-methylcyclohexyl, 4-chloro-3-ethylphenoxycyclohexyl, 3-trifluoromethoxyphenoxycyclohexyl, 3-trifluoromethylcyclohexyl, 4-trifluoromethylcyclohexyl, 3,5-bis-trifluoromethylcyclohexyl, adamantyl, 3-trifluoromethyladamantyl, norbornyl, 3-trifluoromethylnorbornyl, norbornenyl, 7-oxabicyclo[2.2.1]heptan-2-yl, bicyclo[3.1.0]hexan-6-yl, cycloheptyl, cyclooctyl, 2-morpholinyl, 3-morpholinyl, 4-morpholinyl, 1-piperazinyl, 2-piperazinyl, 1-piperidinyl, 2-piperidinyl, 3-piperidinyl, 4-piperidinyl, 1-pyrrolidinyl, 2-pyrrolidinyl, 3-pyrrolidinyl, 2-dioxanyl, 4H-2-pyranyl, 4H-3-pyranyl, 4H-4-pyranyl, 4H-pyran-4-one-2-yl, 4H-pyran-4-one-3-yl, 2-tetrahydrofuranyl, 3-tetrahydrofuranyl, 2-tetrahydropyranyl, 3-tetrahydropyranyl, 4-

tetrahydropyranyl, 2-tetrahydrothienyl, and 3-tetrahydrothienyl, wherein each ring carbon may be optionally substituted with R_{30}, a ring carbon other than the ring carbon at the point of attachment of A to Z may be optionally substituted with oxo provided that no more than one ring carbon is substituted by oxo at the same time, ring carbon and nitrogen atoms adjacent to the carbon atom at the point of attachment may be optionally substituted with R_9 or R_{13}. a ring carbon or nitrogen atom adjacent to the R_9 position and two atoms from the point of attachment may be substituted with R_{10}, a ring carbon or nitrogen atom adjacent to the R_{13} position and two atoms from the point of attachment may be substituted with R_{12}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{10} position may be substituted with R_{11}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{12} position may be substituted with R_{32}, and a ring carbon or nitrogen atom four atoms from the point of attachment and adjacent to the R_{11} and R_{32} positions may be substituted with R_{31};

R_1 is selected from the group consisting of trifluoromethyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, difluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

R_2 is selected from the group consisting of hydrido, methyl, ethyl, phenyl, 4-trifluoromethylphenyl, trifluoromethoxymethyl, 1,1,2,2-tetrafluoroethoxymethyl, difluoromethyl, pentafluoroethyl, trifluoromethyl, and 2,2,3,3,3-pentafluoropropyl;

R_3 is selected from the group consisting of hydrido, phenyl, 4-trifluoromethylphenyl, methyl, trifluoromethyl, difluoromethyl, and chlorodifluoromethyl;

Y and Z are independently selected from a covalent single bond and methylene;

R_4 and R_8 are independently selected from the group consisting of hydrido and fluoro;

R_9 and R_{13} are fluoro;

R_5, R_{10} and R_{12} are independently selected from the group consisting of benzyloxy, 5-bromo-2-fluorophenoxy, 4-bromo-3-fluorophenoxy, 3-bromobenzyloxy, 4-bromophenoxy,4-butoxyphenoxy, 3-chlorobenzyloxy, 2-chlorophenoxy, 4-chloro-3-ethylphenoxy, 4-chloro-3-methylphenoxy, 2-chloro-4-fluorophenoxy, 4-chloro-2-fluorophenoxy, 4-chlorophenoxy, 3-chloro-4-ethylphenoxy, 3-chloro-4-methylphenoxy, 3-chloro-4-fluorophenoxy, 4-chloro-3-fluorophenoxy, 4-chlorophenylamino, 5-chloropyrid-3-yloxy, cyclobutoxy, cyclobutyl, cyclohexylmethoxy, cyclopentoxy, cyclopentyl, cyclopentylcarbonyl, cyclopropylmethoxy, 2,3-dichlorophenoxy, 2,4-dichlorophenoxy, 2,4-dichlorophenyl, 3,5-dichlorophenyl, 3,5-dichlorobenzyl, 3,4-dichlorophenoxy, 3,4-difluorophenoxy,2,3-difluorobenzyloxy, 3,5-difluorobenzyloxy, difluoromethoxy, 3,5-difluorophenoxy, 3,4-difluorophenyl, 2,3-difluorophenoxy, 2,4-difluorophenoxy, 2,5-difluorophenoxy, 3,5-dimethoxyphenoxy,3-dimethylaminophenoxy, 3,4-dimethylbenzyloxy, 3,5-dimethylbenzyloxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 1,3-dioxolan-2-yl, 3-ethylbenzyloxy, 3-ethylphenoxy, 4-ethylaminophenoxy, 3-ethyl-5-methylphenoxy, 4-fluoro-3-methylbenzyl, 4-fluorobenzyloxy, 2-fluoro-3-methylphenoxy, 3-fluoro-4-methylphenoxy, 3-fluorophenoxy, 3-fluoro-2-nitrophenoxy, 2-fluoro-3-trifluoromethylbenzyloxy, 3-fluoro-5-trifluoromethylbenzyloxy, 2-fluorophenoxy, 4-fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2-fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4-trifluoromethylphenoxy, 2-furyl, 3-furyl, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, 2-hydroxy-3,3,3-trifluoropropoxy, isobutoxy, isobutyl, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, isopropoxy, 3-isopropylbenzyloxy, 3-isopropylphenoxy, isopropylthio, 4-isopropyl-3-methylphenoxy, 3-isothiazolyl, 4-isothiazolyl, 5-isothiazolyl, 3-methoxybenzyl, 4-methoxyphenylamino, 3-methylbenzyloxy, 4-methylbenzyloxy, 3-methylphenoxy, 3-methyl-4-methylthiophenoxy, 4-methylphenoxy,

1-methylpropoxy, 2-methylpyrid-5-yloxy, 4-methylthiophenoxy, 2-naphthyloxy, 2-nitrophenoxy, 4-nitrophenoxy, 3-nitrophenyl, 2-oxazolyl, 4-oxazolyl, 5-oxazolyl, pentafluoroethyl, pentafluoroethylthio, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, phenoxy, phenylamino, 1-phenylethoxy, 4-propylphenoxy, 4-propoxyphenoxy, thiophen-3-yl,tert -butoxy, 3-tert -butylphenoxy, 4-tert -butylphenoxy, 1,1,2,2-tetrafluoroethoxy, tetrahydrofuran-2-yl, 2-(5,6,7,8-tetrahydronaphthyloxy), thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, thiophen-2-yl, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, 3,3,3-trifluoro-2-hydroxypropyl, trifluoromethoxy, 3-trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, 4-trifluoromethoxyphenoxy, 3-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, 3-trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3-trifluoromethylphenyl, 2,3,4-trifluorophenoxy, 2,3,5-trifluorophenoxy, 3,4,5-trimethylphenoxy, 3-difluoromethoxyphenoxy, 3-pentafluoroethylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 3-trifluoromethylthiophenoxy, 3-trifluoromethylthiobenzyloxy, and trifluoromethylthio;

R_6, R_{11}, R_{31}, and R_{32} are independently selected from the group consisting of chloro, fluoro, hydrido, pentafluoroethyl, 1,1,2,2-tetrafluoroethoxy, and trifluoromethyl;

R_7 is selected from the group consisting of hydrido, fluoro, and trifluoromethyl;

R_{30} is selected from the group consisting of chloro, ethyl, methyl, propyl, fluoro, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, isobutyl, isopropyl, pentafluoroethyl, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, *sec*-butyl, 1,1,2,2-tetrafluoroethoxy, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, trifluoromethoxy, and trifluoromethyl.

6. The compound as recited in Claim 5 or a pharmaceutically acceptable salt thereof, wherein;

n is the integer 1;

A is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 4-methylcyclohexyl, 4-chloro-3-ethylphenoxycyclohexyl, 3-trifluoromethoxyphenoxycyclohexyl, 3-trifluoromethylcyclohexyl, 4-trifluoromethylcyclohexyl, 3,5-bis-trifluoromethylcyclohexyl, adamantyl, 3-trifluoromethyladamantyl, norbornyl, 3-trifluoromethylnorbornyl, norbornenyl, 7-oxabicyclo[2.2.1]heptan-2-yl, bicyclo[3.1.0]hexan-6-yl, 2-tetrahydrofuranyl, 3-tetrahydrofuranyl, 2-tetrahydropyranyl, 3-tetrahydropyranyl, 4-tetrahydropyranyl, 2-tetrahydrothienyl, and 3-tetrahydrothienyl, wherein a ring carbon other than the ring carbon at the point of attachment of A to Z may be optionally substituted with oxo provided that no more than one ring carbon is substituted by oxo at the same time, ring carbon and nitrogen atoms adjacent to the carbon atom at the point of attachment may be optionally substituted with R_9 or R_{13}, a ring carbon or nitrogen atom adjacent to the R_9 position and two atoms from the point of attachment may be substituted with R_{10}, a ring carbon or nitrogen atom adjacent to the R_{13} position and two atoms from the point of attachment may be substituted with R_{12}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{10} position may be substituted with R_{11}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{12} position may be substituted with R_{32}, and a ring carbon or nitrogen atom four atoms from the point of attachment and adjacent to the R_{11} and R_{32} positions may be substituted with R_{31};

R_1 is selected from the group consisting of trifluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

R_2 is hydrido, pentafluoroethyl, and trifluoromethyl;

R_3 is selected from the group consisting of hydrido, methyl, trifluoromethyl, and difluoromethyl

Y is methylene;

Z is a covalent single bond;

R_4 and R_8 are independently selected from the group consisting of hydrido and fluoro:

R_9 and R_{13} are fluoro;

R_5, R_{10} and R_{12} are independently selected from the group consisting of 5-bromo-2-fluorophenoxy, 4-chloro-3-ethylphenoxy, cyclopentyl, 2,3-dichlorophenoxy, 3,4-dichlorophenoxy, 3-difluoromethoxyphenoxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 3-ethylphenoxy, 3-ethyl-5-methylphenoxy, 4-fluoro-3-methylphenoxy, 4-fluorophenoxy, 2-furyl, isobutyl, isopropoxy, 3-isopropylphenoxy, 3-methylphenoxy, pentafluoroethyl, 3-pentafluoroethylphenoxy, 3-tert -butylphenoxy, 1,1,2,2-tetrafluoroethoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 2-(5,6,7,8-tetrahydronaphthyloxy),trifluoromethoxy, 3-trifluoromethoxybenzyloxy,3-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, trifluoromethylthio, and 3-trifluoromethylthiophenoxy;

R_6, R_{11}, R_{31}, and R_{32} are independently selected from the group consisting of chloro, fluoro, hydrido, pentafluoroethyl, 1,1,2,2-tetrafluoroethoxy, and trifluoromethyl;

R_7 is selected from the group consisting of hydrido and fluoro.

7. The compound as recited in Claim 5 or a pharmaceutically acceptable salt thereof, wherein;

n is the integer 1;

A is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 4-methylcyclohexyl, 4-chloro-3-ethylphenoxycyclohexyl, 3-trifluoromethoxyphenoxycyclohexyl, 3-trifluoromethylcyclohexyl, 4-trifluoromethylcyclohexyl, 3,5-bis-trifluoromethylcyclohexyl, adamantyl, 3-trifluoromethyladamantyl, norbornyl, 3-trifluoromethylnorbornyl, norbornenyl, 7-oxabicyclo[2.2.1]heptan-2-yl, bicyclo[3.1.0]hexan-6-yl, 2-tetrahydrofuranyl, 3-tetrahydrofuranyl, 2-tetrahydropyranyl, 3-tetrahydropyranyl, 4-tetrahydropyranyl, 2-tetrahydrothienyl, and 3-tetrahydrothienyl, wherein a ring carbon other than the ring carbon at the point of attachment of A to Z may be optionally substituted with oxo provided that no more than one ring carbon is substituted by oxo at the same time, ring carbon and nitrogen atoms adjacent to the carbon atom at the point of attachment may be optionally substituted with R_9 or R_{13}, a ring carbon or nitrogen atom adjacent to the R_9 position and two atoms from the point of attachment may be substituted with R_{10}, a ring carbon or nitrogen atom adjacent to the R_{13} position and two atoms from the point of attachment may be substituted with R_{12}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{10} position may be substituted with R_{11}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{12} position may be substituted with R_{32}, and a ring carbon or nitrogen atom four atoms from the point of attachment and adjacent to the R_{11} and R_{32} positions may be substituted with R_{31};

R_1 is selected from the group consisting of trifluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

R_2 is hydrido, pentafluoroethyl, and trifluoromethyl;

R_3 is selected from the group consisting of hydrido, methyl, trifluoromethyl, and difluoromethyl

Y is a covalent single bond;

Z is methylene;

R_4 and R_8 are independently selected from the group consisting of hydrido and fluoro;

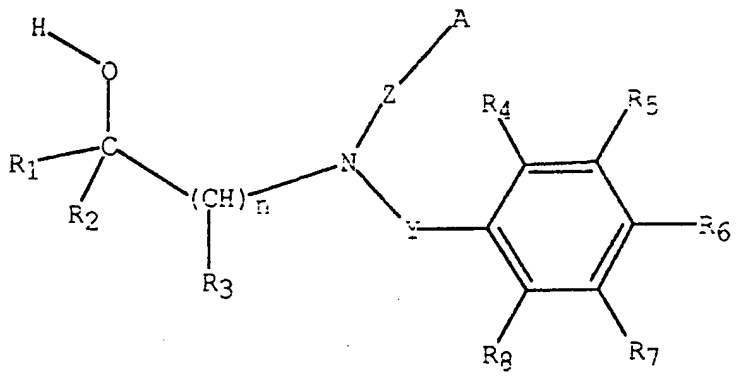
R_9 and R_{13} are fluoro;

R_5, R_{10} and R_{12} are independently selected from the group consisting of 5-bromo-2-fluorophenoxy, 4-chloro-3-ethylphenoxy, cyclopentyl, 2,3-dichlorophenoxy, 3,4-dichlorophenoxy, 3-difluoromethoxyphenoxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 3-ethylphenoxy, 3-ethyl-5-methylphenoxy, 4-fluoro-3-methylphenoxy, 4-fluorophenoxy, 2-furyl, isobutyl, isopropoxy, 3-isopropylphenoxy, 3-methylphenoxy, pentafluoroethyl, 3-pentafluoroethylphenoxy, 3-tert -butylphenoxy, 1,1,2,2-tetrafluoroethoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 2-(5,6,7,8-tetrahydronaphthyloxy),trifluoromethoxy, 3-trifluoromethoxybenzyloxy,3-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, trifluoromethylthio, and 3-trifluoromethylthiophenoxy;

R_6, R_{11}, R_{31}, and R_{32} are independently selected from the group consisting of chloro, fluoro, hydrido, pentafluoroethyl, 1,1,2,2-tetrafluoroethoxy, and trifluoromethyl;

R_7 is selected from the group consisting of hydrido and fluoro.

8. The compound as recited in Claim 2 having the formula of:



or a pharmaceutically acceptable salt thereof, wherein:

n is an integer selected from 1 through 2;

A is selected from the group consisting of C3-C8 alkyl, C3-C8 alkenyl, C3-C8 alkynyl, C3-C8 haloalkyl, C3-C8 haloalkenyl, C3-C6 alkoxy C1-C2 alkyl, and C3-C8 hydroxyhaloalkyl, wherein each member of group A may be optionally substituted at any carbon up to and including 6 atoms from the point of attachment of A to Z with one or more of the group consisting of R_{33}, R_{34}, R_{35}, and R_{36} with the provisos that R_{33}, R_{34}, R_{35}, and R_{36} must not be attached to the carbon directly linking A to Z and that R_{33}, R_{34}, R_{35}, and R_{36} must be selected from other than aryl and heteroaryl when substituting the carbon 2 atoms from Z wherein Z is a single covalent bond;

R_1 is selected from the group consisting of haloalkyl and haloalkoxymethyl;

R_2 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, haloalkoxy, haloalkoxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, and heteroaryl;

R_3 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, and haloalkoxyalkyl;

Y and Z are independently selected from the group consisting of a covalent single bond, oxy and alkylene;

R_4 and R_8 are independently selected from the group consisting of hydrido and halo;

R_5, R_6, R_7, R_{33}, R_{34}, R_{35}, and R_{36} are independently selected from the group consisting of hydrido, alkyl, halo, haloalkyl, haloalkoxy, aryl, alkylthio, arylamino, arylthio, aroyl, arylsulfonyl, aryloxy, aralkoxy, heteroaryloxy, alkoxy, aralkyl, cycloalkoxy, cycloalkylalkoxy, cycloalkylalkanoyl, heteroaryl, cycloalkyl, haloalkylthio, hydroxyhaloalkyl, heteroaralkoxy, heterocyclyloxy, aralkylaryl, heteroaryloxyalkyl, heteroarylthio, and heteroarylsulfonyl;

R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8 are independently selected to form spacer pairs wherein a spacer pair is taken together to form a linear moiety having from 3 through 6 contiguous atoms connecting the points of bonding of said spacer pair members to form a ring selected from the group consisting of a cycloalkenyl ring having 5 through 8 contiguous members, a partially saturated heterocyclyl ring having 5 through 8 contiguous members, a heteroaryl ring having 5 through 6 contiguous members, and an aryl with the proviso that no more than one of the group consisting of spacer pairs R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8, is used at the same time;

9. The compound as recited in Claim 8 or a pharmaceutically acceptable salt thereof, wherein;

n is the integer 1;

A is selected from the group consisting of ethyl, 1-propenyl, propyl, isopropyl, butyl, 2-butenyl, 3-butenyl, *sec*-butyl, isobutyl, 2-methylpropenyl, 1-pentyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, 2-pentyl, 1-methyl-2-butenyl, 1-methyl-3-butenyl, 3-pentyl, 1-ethyl-2-propenyl, 2-methylbutyl, 2-methyl-2-butenyl, 2-methyl-3-butenyl, 3-methylbutyl, 3-methyl-2-butenyl, 3-methyl-3-butenyl, 1-hexyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, 5-hexenyl, 2-hexyl, 1-methyl-2-pentenyl, 1-methyl-3-pentenyl, 1-methyl-4-pentenyl, 3-hexyl, 1-

ethyl-2-butenyl, 1-ethyl-3-butenyl, 1-propyl-2-propenyl, 1-heptyl, 2-heptenyl, 3-heptenyl, 4-heptenyl, 5-heptenyl, 6-heptenyl, 2-heptyl, 1-methyl-2-hexenyl, 1-methyl-3-hexenyl, 1-methyl-4-hexenyl, 1-methyl-5-hexenyl, 3-heptyl, 1-ethyl-2-pentenyl, 1-ethyl-3-pentenyl, 1-ethyl-4-pentenyl, 1-butyl-2-propenyl, 1-octyl, 2-octenyl, 3-octenyl, 4-octenyl, 5-octenyl, 6-octenyl, 7-octenyl, 2-octyl, 1-methyl-2-heptenyl, 1-methyl-3-heptenyl, 1-methyl-4-heptenyl, 1-methyl-5-heptenyl, 1-methyl-6-heptenyl, 1-methyl-4-heptenyl, 1-methyl-6-heptenyl, 1-methyl-2-heptenyl, 3-octyl, 1-ethyl-2-hexenyl, 1-ethyl-3-hexenyl, 1-ethyl-4-hexenyl, 1-ethyl-5-hexenyl, 1-pentyl-2-propenyl, 4-octyl, 1-propyl-2-pentenyl, 1-propyl-3-pentenyl, 1-propyl-4-pentenyl, 1-butyl-2-butenyl, 1-butyl-3-butenyl, 2,2-difluoropropyl, 4-trifluoromethyl-5,5,5-trifluoropentyl, 4-trifluoromethylpentyl, 5,5,6,6,6-pentafluorohexyl, and 3,3,3-trifluoropropyl, wherein each member of group A may be optionally substituted at any carbon up to and including 6 atoms from the point of attachment of A to Z with one or more of the group consisting of R_{33}, R_{34}, R_{35}, and R_{36} with the provisos that R_{33}, R_{34}, R_{35}, and R_{36} must not be attached to the carbon directly linking A to Z and that R_{33}, R_{34}, R_{35}, and R_{36} must be selected from other than aryl and heteroaryl when substituting the carbon 2 atoms from Z wherein Z is a single covalent bond;

R_1 is selected from the group consisting of trifluoromethyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, difluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

R_2 is selected from the group consisting of hydrido, methyl, ethyl, phenyl, 4-trifluoromethylphenyl, trifluoromethoxymethyl, 1,1,2,2-tetrafluoroethoxymethyl, difluoromethyl, pentafluoroethyl, trifluoromethyl, and 2,2,3,3,3-pentafluoropropyl;

R_3 is selected from the group consisting of hydrido, phenyl, 4-trifluoromethylphenyl, methyl, trifluoromethyl, difluoromethyl, and chlorodifluoromethyl;

Y and Z are independently selected from a covalent single bond and methylene;

R_4 and R_8 are independently selected from the group consisting of hydrido and fluoro;

R_5, R_{33}, R_{34}, R_{35}, and R_{36} are independently selected from the group consisting of benzyloxy, 5-bromo-2-fluorophenoxy, 4-bromo-3-fluorophenoxy, 3-bromobenzyloxy, 4-bromophenoxy, 4-butoxyphenoxy, 3-chlorobenzyloxy, 2-chlorophenoxy, 4-chloro-3-ethylphenoxy, 4-chloro-3-methylphenoxy, 2-chloro-4-fluorophenoxy, 4-chloro-2-fluorophenoxy, 4-chlorophenoxy, 3-chloro-4-ethylphenoxy, 3-chloro-4-methylphenoxy, 3-chloro-4-fluorophenoxy, 4-chloro-3-fluorophenoxy, 4-chlorophenylamino, 5-chloropyrid-3-yloxy, cyclobutoxy, cyclobutyl, cyclohexylmethoxy, cyclopentoxy, cyclopentyl, cyclopentylcarbonyl, cyclopropylmethoxy, 2,3-dichlorophenoxy, 2,4-dichlorophenoxy, 2,4-dichlorophenyl, 3,5-dichlorophenyl, 3,5-dichlorobenzyl, 3,4-dichlorophenoxy, 3,4-difluorophenoxy,2,3-difluorobenzyloxy, 3,5-difluorobenzyloxy, difluoromethoxy, 3,5-difluorophenoxy, 3,4-difluorophenyl, 2,3-difluorophenoxy, 2,4-difluorophenoxy, 2,5-difluorophenoxy, 3,5-dimethoxyphenoxy,3-dimethylaminophenoxy, 3,4-dimethylbenzyloxy, 3,5-dimethylbenzyloxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 1,3-dioxolan-2-yl, 3-ethylbenzyloxy, 3-ethylphenoxy, 4-ethylaminophenoxy, 3-ethyl-5-methylphenoxy, 4-fluoro-3-methylbenzyl, 4-fluorobenzyloxy, 2-fluoro-3-methylphenoxy, 3-fluoro-4-methylphenoxy, 3-fluorophenoxy, 3-fluoro-2-nitrophenoxy, 2-fluoro-3-trifluoromethylbenzyloxy, 3-fluoro-5-trifluoromethylbenzyloxy, 2-fluorophenoxy, 4-fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2-fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4-trifluoromethylphenoxy, 2-furyl, 3-furyl, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, 2-hydroxy-3,3,3-trifluoropropoxy, isobutoxy, isobutyl, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, isopropoxy, 3-isopropylbenzyloxy, 3-isopropylphenoxy, isopropylthio, 4-isopropyl-3-methylphenoxy, 3-isothiazolyl, 4-isothiazolyl, 5-isothiazolyl, 3-methoxybenzyl, 4-methoxyphenylamino, 3-methylbenzyloxy, 4-methylbenxyloxy, 3-methylphenoxy, 3-methyl-4-methylthiophenoxy, 4-methylphenoxy, 1-methylpropoxy, 2-methylpyrid-5-yloxy, 4-methylthiophenoxy,

2-naphthyloxy, 2-nitrophenoxy, 4-nitrophenoxy, 3-nitrophenyl, 2-oxazolyl, 4-oxazolyl, 5-oxazolyl, pentafluoroethyl, pentafluoroethylthio, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, phenoxy, phenylamino, 1-phenylethoxy, 4-propylphenoxy, 4-propoxyphenoxy, thiophen-3-yl,tert -butoxy, 3-tert -butylphenoxy, 4-tert -butylphenoxy, 1,1,2,2-tetrafluoroethoxy, tetrahydrofuran-2-yl, 2-(5,6,7,8-tetrahydronaphthyloxy), thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, thiophen-2-yl, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, 3,3,3-trifluoro-2-hydroxypropyl, trifluoromethoxy, 3-trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, 4-trifluoromethoxyphenoxy, 3-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, 3-trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3-trifluoromethylphenyl, 2,3,4-trifluorophenoxy, 2,3,5-trifluorophenoxy, 3,4,5-trimethylphenoxy, 3-difluoromethoxyphenoxy, 3-pentafluoroethylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 3-trifluoromethylthiophenoxy, 3-trifluoromethylthiobenzyloxy, and trifluoromethylthio;

R_6 is selected from the group consisting of chloro, fluoro, hydrido, pentafluoroethyl, 1,1,2,2-tetrafluoroethoxy, and trifluoromethyl;

R_7 is selected from the group consisting of hydrido, fluoro, and trifluoromethyl.

10. The compound as recited in Claim 9 or a pharmaceutically acceptable salt thereof, wherein;

n is the integer 1;

A is selected from the group consisting of 1-propenyl, propyl, isopropyl, butyl, 2-butenyl, 3-butenyl, *sec*-butyl, isobutyl, 2-methylpropenyl, 1-pentyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, 2-pentyl, 1-methyl-2-butenyl, 1-methyl-3-butenyl, 3-pentyl, 1-ethyl-2-propenyl, 2-methylbutyl, 2-methyl-2-butenyl, 2-methyl-3-butenyl, 3-methylbutyl, 3-methyl-2-butenyl, 3-methyl-3-butenyl, 1-hexyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, 5-hexenyl, 2-hexyl, 1-

methyl-2-pentenyl, 1-methyl-3-pentenyl, 1-methyl-4-pentenyl, 3-hexyl, 1-ethyl-2-butenyl, 1-ethyl-3-butenyl, 1-propyl-2-propenyl, 1-ethyl-2-pentenyl, 1-ethyl-3-pentenyl, 1-ethyl-4-pentenyl, 1-butyl-2-propenyl, 1-ethyl-2-hexenyl, 1-ethyl-3-hexenyl, 1-ethyl-4-hexenyl, 1-ethyl-5-hexenyl, 1-pentyl-2-propenyl,1-propyl-2-pentenyl, 1-propyl-3-pentenyl, 1-propyl-4-pentenyl, 1-butyl-2-butenyl, 1-butyl-3-butenyl, 2,2-difluoropropyl, 4-trifluoromethyl-5,5,5-trifluoropentyl, 4-trifluoromethylpentyl, 5,5,6,6,6-pentafluorohexyl, and 3,3,3-trifluoropropyl, wherein each member of group A may be optionally substituted at any carbon up to and including 6 atoms from the point of attachment of A to Z with one or more of the group consisting of R_{33}, R_{34}, R_{35}, and R_{36} with the provisos that R_{33}, R_{34}, R_{35}, and R_{36} must not be attached to the carbon directly linking A to Z and that R_{33}, R_{34}, R_{35}, and R_{36} must be selected from other than aryl and heteroaryl when substituting the carbon 2 atoms from Z wherein Z is a single covalent bond;

R_1 is selected from the group consisting of trifluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

R_2 is hydrido, pentafluoroethyl, and trifluoromethyl;

R_3 is selected from the group consisting of hydrido, methyl, trifluoromethyl, and difluoromethyl

Y is a covalent single bond;

Z is methylene;

R_4 and R_8 are independently selected from the group consisting of hydrido and fluoro;

R_5, R_{33}, R_{34}, R_{35}, and R_{36} are independently selected from the group consisting of 5-bromo-2-fluorophenoxy, 4-chloro-3-ethylphenoxy, cyclopentyl, 2,3-dichlorophenoxy, 3,4-dichlorophenoxy, 3-difluoromethoxyphenoxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 3-ethylphenoxy, 3-ethyl-5-methylphenoxy, 4-fluoro-3-methylphenoxy,

4-fluorophenoxy, 2-furyl, isobutyl, isopropoxy, 3-isopropylphenoxy, 3-methylphenoxy, pentafluoroethyl, 3-pentafluoroethylphenoxy, 3-tert-butylphenoxy, 1,1,2,2-tetrafluoroethoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 2-(5,6,7,8-tetrahydronaphthyloxy), trifluoromethoxy, 3-trifluoromethoxybenzyloxy,3-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, trifluoromethylthio, and 3-trifluoromethylthiophenoxy;

R_6 is selected from the group consisting of fluoro and hydrido;

R_7 is selected from the group consisting of hydrido and fluoro.

11. The compound as recited in Claim 9 or a pharmaceutically acceptable salt thereof, wherein;

n is the integer 1;

A is selected from the group consisting of 1-propenyl, propyl, isopropyl, butyl, 2-butenyl, 3-butenyl, *sec*-butyl, isobutyl, 2-methylpropenyl, 1-pentyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, 2-pentyl, 1-methyl-2-butenyl, 1-methyl-3-butenyl, 3-pentyl, 1-ethyl-2-propenyl, 2-methylbutyl, 2-methyl-2-butenyl, 2-methyl-3-butenyl, 3-methylbutyl, 3-methyl-2-butenyl, 3-methyl-3-butenyl, 1-hexyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, 5-hexenyl, 2-hexyl, 1-methyl-2-pentenyl, 1-methyl-3-pentenyl, 1-methyl-4-pentenyl, 3-hexyl, 1-ethyl-2-butenyl, 1-ethyl-3-butenyl, 1-propyl-2-propenyl, 1-ethyl-2-pentenyl, 1-ethyl-3-pentenyl, 1-ethyl-4-pentenyl, 1-butyl-2-propenyl, 1-ethyl-2-hexenyl, 1-ethyl-3-hexenyl, 1-ethyl-4-hexenyl, 1-ethyl-5-hexenyl, 1-pentyl-2-propenyl,1-propyl-2-pentenyl, 1-propyl-3-pentenyl, 1-propyl-4-pentenyl, 1-butyl-2-butenyl, 1-butyl-3-butenyl, 2,2-difluoropropyl, 4-trifluoromethyl-5,5,5-trifluoropentyl, 4-trifluoromethylpentyl, 5,5,6,6,6-pentafluorohexyl, and 3,3,3-trifluoropropyl, wherein each member of group A may be optionally substituted at any carbon up to and including 6 atoms from the point of attachment of A to Z with one or more of the group consisting of R_{33}, R_{34}, R_{35}, and R_{36} with the provisos that R_{33}, R_{34}, R_{35}, and R_{36} must not be attached to the carbon directly linking A to Z and that R_{33}, R_{34}, R_{35}, and R_{36}

must be selected from other than aryl and heteroaryl when substituting the carbon 2 atoms from Z wherein Z is a single covalent bond;

R_1 is selected from the group consisting of trifluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

R_2 is hydrido, pentafluoroethyl, and trifluoromethyl;

R_3 is selected from the group consisting of hydrido, methyl, trifluoromethyl, and difluoromethyl

Y is methylene;

Z is a covalent single bond;

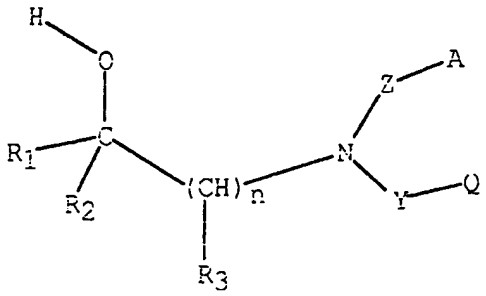
R_4 and R_8 are independently selected from the group consisting of hydrido and fluoro;

R_5, R_{33}, R_{34}, R_{35}, and R_{36} are independently selected from the group consisting of 5-bromo-2-fluorophenoxy, 4-chloro-3-ethylphenoxy, cyclopentyl, 2,3-dichlorophenoxy, 3,4-dichlorophenoxy, 3-difluoromethoxyphenoxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 3-ethylphenoxy, 3-ethyl-5-methylphenoxy, 4-fluoro-3-methylphenoxy, 4-fluorophenoxy, 2-furyl, isobutyl, isopropoxy, 3-isopropylphenoxy, 3-methylphenoxy, pentafluoroethyl, 3-pentafluoroethylphenoxy, 3-tert-butylphenoxy, 1,1,2,2-tetrafluoroethoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 2-(5,6,7,8-tetrahydronaphthyloxy), trifluoromethoxy, 3-trifluoromethoxybenzyloxy,3-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, trifluoromethylthio, and 3-trifluoromethylthiophenoxy;

R_6 is selected from the group consisting of fluoro and hydrido;

R_7 is selected from the group consisting of hydrido and fluoro.

12. The compound as recited in Claim 1 having the formula of:

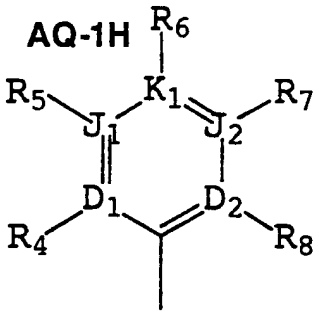


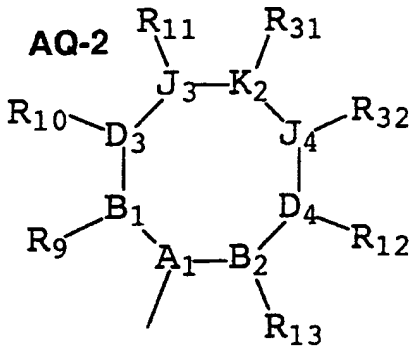
or a pharmaceutically acceptable salt thereof, wherein;

n is an integer selected from 1 through 2;

A and Q are independently selected from the group consisting of

$-CH_2(CR_{37}R_{38})_v-(CR_{33}R_{34})_u-T-(CR_{35}R_{36})_w-H$,

AQ-1H 

and AQ-2 

with the provisos that one of A and Q must be AQ-1H and that one of A and Q must be selected from the group consisting of AQ-2 and

$-CH_2(CR_{37}R_{38})_v-(CR_{33}R_{34})_u-T-(CR_{35}R_{36})_w-H$;

T is selected from the group consisting of a single covalent bond, O, S, S(O), $S(O)_2$, $C(R_{33})=C(R_{35})$, and C≡C;

v is an integer selected from 0 through 1 with the proviso that v is 1 when any one of R_{33}, R_{34}, R_{35}, and R_{36} is aryl or heteroaryl;

u and w are integers independently selected from 0 through 6;

A_1 is $C(R_{30})$;

D_1, D_2, J_1, J_2 and K_1 are independently selected from the group consisting of C, N, O, S and a covalent bond with the provisos that no more than one of D_1, D_2, J_1, J_2 and K_1 is a covalent bond, no more than one of D_1, D_2, J_1, J_2 and K_1 is O, no more than one of D_1, D_2, J_1, J_2 and K_1 is S, one of D_1, D_2, J_1, J_2 and K_1 must be a covalent bond when two of D_1, D_2, J_1, J_2 and K_1 are O and S, and no more than four of D_1, D_2, J_1, J_2 and K_1 are N;

B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are independently selected from the group consisting of C, $C(R_{30})$, N, O, S and a covalent bond with the provisos that no more than 5 of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are a covalent bond, no more than two of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are O, no more than two of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are S, no more than two of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are simultaneously O and S, and no more than two of B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are N;

B_1 and D_3, D_3 and J_3, J_3 and K_2, K_2 and J_4, J_4 and D_4, and D_4 and B_2 are independently selected to form an in-ring spacer pair wherein said spacer pair is selected from the group consisting of $C(R_{33})=C(R_{35})$ and N=N with the provisos that AQ-2 must be a ring of at least five contiguous members, that no more than two of the group of said spacer pairs are simultaneously $C(R_{33})=C(R_{35})$, and that no more than one of the group of said spacer pairs is N=N unless the other spacer pairs are other than $C(R_{33})=C(R_{35})$, O, N, and S;

R_1 is selected from the group consisting of haloalkyl and haloalkoxymethyl;

R_2 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, haloalkoxy, haloalkoxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, and heteroaryl;

R_3 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, and haloalkoxyalkyl;

Y is selected from the group consisting of a covalent single bond, $(CH_2)_q$ wherein q is an integer selected from 1 through 2, and $(CH_2)_j$-O-$(CH_2)_k$ wherein j and k are integers independently selected from 0 through 1;

Z is selected from the group consisting of covalent single bond, $(CH_2)_q$ wherein q is an integer selected from 1 through 2, and $(CH_2)_j$-O-$(CH_2)_k$ wherein j and k are integers independently selected from 0 through 1;

R_{30} is selected from the group consisting of hydrido, alkoxy, alkoxyalkyl, halo, haloalkyl, alkylamino, alkylthio, alkylthioalkyl, alkyl, alkenyl, haloalkoxy, and haloalkoxyalkyl with the proviso that R_{30} is selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen;

R_{30}, when bonded to A_1, is taken together to form an intra-ring linear spacer connecting the A_1-carbon at the point of attachment of R_{30} to the point of bonding of a group selected from the group consisting of R_{10}, R_{11}, R_{12}, R_{31}, and R_{32} wherein said intra-ring linear spacer is selected from the group consisting of a covalent single bond and a spacer moiety having from 1 through 6 contiguous atoms to form a ring selected from the group consisting of a cycloalkyl having from 3 through 10 contiguous members, a cycloalkenyl having from 5 through 10 contiguous members, and a heterocyclyl having from 5 through 10 contiguous members;

R_{30}, when bonded to A_1, is taken together to form an intra-ring branched spacer connecting the A_1-carbon at the point of attachment of R_{30} to the points of bonding of each member of any one of substituent pairs selected from the group consisting of subsitituent pairs R_{10} and R_{11}, R_{10} and R_{31}, R_{10} and R_{32}, R_{10} and R_{12}, R_{11} and R_{31}, R_{11} and R_{32}, R_{11} and R_{12}, R_{31} and R_{32}, R_{31} and R_{12}, and R_{32} and R_{12} and wherein said intra-ring branched spacer is selected to form two rings selected from the group consisting of cycloalkyl having from 3 through 10 contiguous members, cycloalkenyl having from 5 through 10 contiguous members, and heterocyclyl having from 5 through 10 contiguous members;

R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, R_{32} , R_{33}, R_{34}, R_{35}, and R_{36} are independently selected from the group consisting of hydrido, carboxy, heteroaralkylthio, heteroaralkoxy, cycloalkylamino, acylalkyl, acylalkoxy, aroylalkoxy, heterocyclyloxy, aralkylaryl, aralkyl, aralkenyl, aralkynyl, heterocyclyl, perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, aralkylsulfinyl, aralkylsulfinylalkyl, halocycloalkyl, halocycloalkenyl, cycloalkylsulfinyl, cycloalkylsulfinylalkyl, cycloalkylsulfonyl, cycloalkylsulfonylalkyl, heteroarylamino, N-heteroarylamino-N-alkylamino, heteroarylaminoalkyl,haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, haloalkoxylalkyl, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, cycloalkoxyalkyl, cycloalkylalkoxy, cycloalkenyloxyalkyl, cycloalkylenedioxy, halocycloalkoxy, halocycloalkoxyalkyl, halocycloalkenyloxy, halocycloalkenyloxyalkyl, hydroxy, amino, thio, nitro, lower alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylthioalkyl, heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, arylsulfonylalkyl, heteroarylsulfinylalkyl, heteroarylsulfonylalkyl, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfinylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, monoarylamidosulfonyl, arylsulfonamido, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl,

arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, heterocyclylsulfonyl, heterocyclylthio, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, alkenyloxy, alkenyloxyalky, alkylenedioxy, haloalkylenedioxy, cycloalkyl, cycloalkylalkanoyl, cycloalkenyl, lower cycloalkylalkyl, lower cycloalkenylalkyl, halo, haloalkyl, haloalkenyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydoxyheteroaralkyl, haloalkoxyalkyl, aryl, heteroaralkynyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, arylalkenyl, heteroarylalkenyl, carboxyalkyl, carboalkoxy, alkoxycarboxamido, alkylamidocarbonylamido, arylamidocarbonylamido, carboalkoxyalkyl, carboalkoxyalkenyl, carboaralkoxy, carboxamido, carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl with the provisos that

R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, R_{32}, R_{33}, R_{34}, R_{35}, and R_{36} are each independently selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen, that no more than three of the R_{33} and R_{34} substituents are simultaneously selected from other than the group consisting of of hydrido and halo, and that no more than three of the R_{35} and R_{36} substituents are simultaneously selected from other than the group consistubg of hydrido and halo;

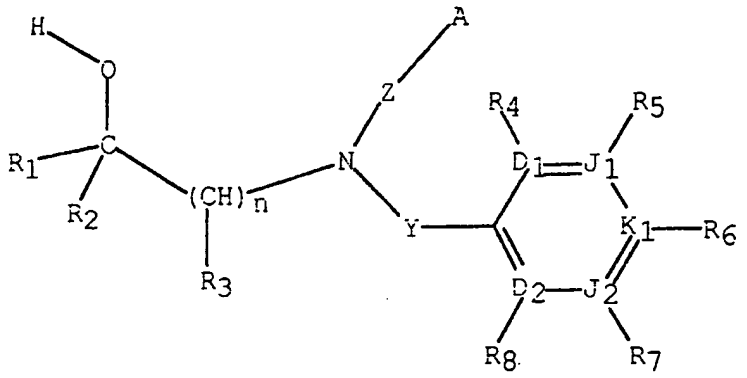
R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, and R_{32} are independently selected to be oxo with the provisos that B_1, B_2, D_3, D_4, J_3, J_4 and K_2 are independently selected from the group consisting of C and S, no more than two of R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, and R_{32} are simultaneously oxo, and that R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{31}, and R_{32} are each independently selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen;

R_4 and R_5, R_5 and R_6, R_6 and R_7, R_7 and R_8, R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{31}, R_{31} and R_{32}, R_{32} and R_{12}, and R_{12} and R_{13} are independently selected to form spacer pairs wherein a spacer pair is taken together to form a linear moiety having from 3 through 6 contiguous atoms connecting the points of bonding of said spacer pair members to form a ring selected from the group consisting of a cycloalkenyl ring having 5 through 8 contiguous members, a partially saturated heterocyclyl ring having 5 through 8 contiguous members, a heteroaryl ring having 5 through 6 contiguous members, and an aryl with the provisos that no more than one of the group consisting of spacer pairs R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8, is used at the same time and that no more than one of the group consisting of spacer pairs R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{31}, R_{31} and R_{32}, R_{32} and R_{12}, and R_{12} and R_{13} is used at the same time;

R_9 and R_{11}, R_9 and R_{12}, R_9 and R_{13}, R_9 and R_{31}, R_9 and R_{32}, R_{10} and R_{12}, R_{10} and R_{13}, R_{10} and R_{31}, R_{10} and R_{32}, R_{11} and R_{12}, R_{11} and R_{13}, R_{11} and R_{32}, R_{12} and R_{31}, R_{13} and R_{31}, and R_{13} and R_{32} are independently selected to form a spacer pair wherein said spacer pair is taken together to form a linear spacer moiety selected from the group consisting of a covalent single bond and a moiety having from 1 through 3 contiguous atoms to form a ring selected from the group consisting of a cycloalkyl having from 3 through 8 contiguous members, a cycloalkenyl having from 5 through 8 contiguous members, a saturated heterocyclyl having from 5 through 8 contiguous members and a partially saturated heterocyclyl having from 5 through 8 contiguous members with the provisos that no more than one of said group of spacer pairs is used at the same time;

R_{37} and R_{38} are independently selected from the group consisting of hydrido, alkoxy, alkoxyalkyl, hydroxy, amino, thio, halo, haloalkyl, alkylamino, alkylthio, alkylthioalkyl, cyano, alkyl, alkenyl, haloalkoxy, and haloalkoxyalkyl.

13. The compound as recited in Claim 12 having the formula of:



or a pharmaceutically acceptable salt thereof, wherein;

n is an integer selected from 1 through 2;

A is selected from the group consisting of C3-C10 cycloalkyl, C5-C10 cycloalkenyl, C4-C9 saturated heterocyclyl, and C4-C9 partially saturated heterocyclyl, wherein each ring carbon may be optionally substituted with R_{30}, a ring carbon other than the ring carbon at the point of attachment of A to Z may be optionally substituted with oxo provided that no more than one ring carbon is substituted by oxo at the same time, ring carbon and nitrogen atoms adjacent to the carbon atom at the point of attachment may be optionally substituted with R_9 or R_{13}, a ring carbon or nitrogen atom adjacent to the R_9 position and two atoms from the point of attachment may be substituted with R_{10}, a ring carbon or nitrogen atom adjacent to the R_{13} position and two atoms from the point of attachment may be substituted with R_{12}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{10} position may be substituted with R_{11}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{12} position may be substituted with R_{32}, and a ring carbon or nitrogen atom four atoms from

the point of attachment and adjacent to the R_{11} and R_{32} positions may be substituted with R_{31};

D_1, D_2, J_1, J_2 and K_1 are independently selected from the group consisting of C, N, O, S and a covalent bond with the provisos that no more than one of D_1, D_2, J_1, J_2 and K_1 is a covalent bond, no more than one of D_1, D_2, J_1, J_2 and K_1 is O, no more than one of D_1, D_2, J_1, J_2 and K_1 is S, one of D_1, D_2, J_1, J_2 and K_1 must be a covalent bond when two of D_1, D_2, J_1, J_2 and K_1 are O and S, and no more than four of D_1, D_2, J_1, J_2 and K_1 are N;

R_1 is selected from the group consisting of haloalkyl and haloalkoxymethyl;

R_2 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, haloalkoxy, haloalkoxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, and heteroaryl;

R_3 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, and haloalkoxyalkyl;

Y and Z are independently selected from the group consisting of a covalent single bond, oxy and alkylene;

R_4 and R_8 are independently selected from the group consisting of hydrido and halo;

R_9 and R_{13} are halo;

R_5, R_6, and R_7 are independently selected from the group consisting of hydrido, alkyl, halo, haloalkyl, haloalkoxy, aryl, alkylthio, arylamino, arylthio, aroyl, arylsulfonyl, aryloxy, aralkoxy, heteroaryloxy, alkoxy, aralkyl, cycloalkoxy, cycloalkylalkoxy, cycloalkylalkanoyl, heteroaryl, cycloalkyl, haloalkylthio, hydroxyhaloalkyl, heteroaralkoxy, heterocyclyloxy, aralkylaryl, heteroaryloxyalkyl, heteroarylthio, and heteroarylsulfonyl;

R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8 are independently selected to form spacer pairs wherein a spacer pair is taken together to form a linear moiety having from 3 through 6 contiguous atoms connecting the points of bonding of said spacer pair members to form a ring selected from the group consisting of a cycloalkenyl ring having 5 through 8 contiguous members, a partially saturated heterocyclyl ring having 5 through 8 contiguous members, a heteroaryl ring having 5 through 6 contiguous members, and an aryl with the proviso that no more than one of the group consisting of spacer pairs R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8, is used at the same time;

R_{10}, R_{11}, R_{12}, R_{31}, and R_{32} are independently selected from the group group consisting of alkyl, halo, haloalkyl, haloalkoxy, aryl, alkylthio, arylamino, arylthio, aroyl, arylsulfonyl, aryloxy, aralkoxy, heteroaryloxy, alkoxy, aralkyl, cycloalkoxy, cycloalkylalkoxy, cycloalkylalkanoyl, heteroaryl, cycloalkyl, haloalkylthio, hydroxyhaloalkyl, heteroaralkoxy, heterocyclyloxy, aralkylaryl, heteroaryloxyalkyl, heteroarylthio, and heteroarylsulfonyl;

R_{30} is selected from the group consisting of alkoxy, alkoxyalkyl, halo, haloalkyl, alkylamino, alkylthio, alkylthioalkyl, alkyl, alkenyl, haloalkoxy, and haloalkoxyalkyl.

14. The compound as recited in Claim 13 or a pharmaceutically acceptable salt thereof, wherein;

n is the integer 1;

A is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclopent-2-enyl, cyclopent-3-enyl, cyclohexyl, 4-methylcyclohexyl, 4-chloro-3-ethylphenoxycyclohexyl, 3-trifluoromethoxyphenoxycyclohexyl, 3-trifluoromethylcyclohexyl, 4-trifluoromethylcyclohexyl, 3,5-bis-trifluoromethylcyclohexyl, adamantyl, 3-trifluoromethyladamantyl, norbornyl, 3-trifluoromethylnorbornyl, norbornenyl, 7-oxabicyclo[2.2.1]heptan-2-yl, bicyclo[3.1.0]hexan-6-yl, cyclohex-2-enyl, cyclohex-3-enyl, cycloheptyl, cyclohept-2-enyl, cyclohept-3-enyl, cyclooctyl, cyclooct-2-enyl, cyclooct-3-enyl, cyclooct-4-enyl, 2-

morpholinyl, 3-morpholinyl, 4-morpholinyl, 1-piperazinyl, 2-piperazinyl, 1-piperidinyl, 2-piperidinyl, 3-piperidinyl, 4-piperidinyl, 1-pyrrolidinyl, 2-pyrrolidinyl, 3-pyrrolidinyl, 2-dioxanyl, 2H-2-pyranyl, 2H-3-pyranyl, 2H-4-pyranyl, 4H-2-pyranyl, 4H-3-pyranyl, 4H-4-pyranyl, 2H-pyran-2-one-3-yl, 2H-pyran-2-one-4-yl, 2H-pyran-2-one-5-yl, 4H-pyran-4-one-2-yl, 4H-pyran-4-one-3-yl, 2-tetrahydrofuranyl, 3-tetrahydrofuranyl, 2-tetrahydropyranyl, 3-tetrahydropyranyl, 4-tetrahydropyranyl, 2-tetrahydrothienyl, and 3-tetrahydrothienyl, wherein each ring carbon may be optionally substituted with R_{30}, a ring carbon other than the ring carbon at the point of attachment of A to Z may be optionally substituted with oxo provided that no more than one ring carbon is substituted by oxo at the same time, ring carbon and nitrogen atoms adjacent to the carbon atom at the point of attachment may be optionally substituted with R_9 or R_{13}, a ring carbon or nitrogen atom adjacent to the R_9 position and two atoms from the point of attachment may be substituted with R_{10}, a ring carbon or nitrogen atom adjacent to the R_{13} position and two atoms from the point of attachment may be substituted with R_{12}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{10} position may be substituted with R_{11}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{12} position may be substituted with R_{32}, and a ring carbon or nitrogen atom four atoms from the point of attachment and adjacent to the R_{11} and R_{32} positions may be substituted with R_{31};

D_1, D_2, J_1, J_2 and K_1 are independently selected from the group consisting of C, N, O, S and a covalent bond to form the group consisting of 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrrolyl, 3-pyrrolyl, 2-imidazolyl, 4-imidazolyl, 3-pyrazolyl, 4-pyrazolyl, 1,2,4-triazol-3-yl, 1,2,4-triazol-5-yl, 1,2,4-oxadiazol-3-yl, 1,2,4-oxadiazol-5-yl, 1,3,4-oxadiazol-3-yl, 1,3,4-oxadiazol-5-yl, 3-isothiazolyl, 5-isothiazolyl, 2-oxazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl, 2-

pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl, 4-pyridazinyl, 1,3,5-triazin-2-yl, 1,2,4-triazin-3-yl, 1,2,4-triazin-5-yl, 1,2,4-triazin-6-yl, 1,2,3-triazin-4-yl, 1-indolizinyl, 7-indolizinyl, 1-isoquinolyl, and 2-quinolyl, wherein a ring carbon atom adjacent to the carbon atom at the point of attachment may be optionally substituted with R_4 or R_8, a ring carbon atom adjacent to the R_4 position and two atoms from the point of attachment may be substituted with R5, a ring carbon atom adjacent to the R_8 position and two atoms from the point of attachment may be substituted with R_7, and a ring carbon atom three atoms from the point of attachment and adjacent to the R_5 and R_7 positions may be substituted with R_6;

R_1 is selected from the group consisting of trifluoromethyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, difluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

R_2 is selected from the group consisting of hydrido, methyl, ethyl, propyl, butyl, vinyl, phenyl, 4-trifluoromethylphenyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, difluoromethyl, pentafluoroethyl, trifluoromethyl, and 2,2,3,3,3-pentafluoropropyl;

R_3 is selected from the group consisting of hydrido, phenyl, 4-trifluoromethylphenyl, methyl, ethyl, vinyl, trifluoromethyl, trifluoromethoxymethyl, difluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

Y and Z are independently selected from the group consisting of a covalent single bond, oxy, and methylene with the proviso that only one of Y and Z are simultaneously oxy;

R_4 and R_8 are independently selected from the group consisting of hydrido and fluoro;

R_9 and R_{13} are fluoro;

R_5, R_{10} and R_{12} are independently selected from the group consisting of 4-aminophenoxy, benzoyl, benzyl, benzyloxy, 5-bromo-2-fluorophenoxy, 4-bromo-3-fluorophenoxy, 4-bromo-2-nitrophenoxy, 3-bromobenzyloxy, 4-bromobenzyloxy, 4-bromophenoxy, 5-bromopyrid-2-yloxy, 4-butoxyphenoxy, chloro, 3-chlorobenzyl, 2-chlorophenoxy, 4-chlorophenoxy, 4-chloro-3-ethylphenoxy, 3-chloro-4-fluorobenzyl, 3-chloro-4-fluorophenyl, 3-chloro-2-fluorobenzyloxy, 3-chlorobenzyloxy, 4-chlorobenzyloxy, 4-chloro-3-methylphenoxy, 2-chloro-4-fluorophenoxy, 4-chloro-2-fluorophenoxy, 4-chlorophenoxy, 3-chloro-4-ethylphenoxy, 3-chloro-4-methylphenoxy, 3-chloro-4-fluorophenoxy, 4-chloro-3-fluorophenoxy, 4-chlorophenylamino, 5-chloropyrid-3-yloxy, 2-cyanopyrid-3-yloxy, 4-cyanophenoxy, cyclobutoxy, cyclobutyl, cyclohexoxy, cyclohexylmethoxy, cyclopentoxy, cyclopentyl, cyclopentylcarbonyl, cyclopropyl, cyclopropylmethoxy, cyclopropoxy, 2,3-dichlorophenoxy, 2,4-dichlorophenoxy, 2,4-dichlorophenyl, 3,5-dichlorophenyl, 3,5-dichlorobenzyl, 3,4-dichlorophenoxy, 3,4-difluorophenoxy, 2,3-difluorobenzyloxy, 2,4-difluorobenzyloxy, 3,4-difluorobenzyloxy, 2,5-difluorobenzyloxy, 3,5-difluorophenoxy, 3,4-difluorophenyl, 3,5-difluorobenzyloxy, 4-difluoromethoxybenzyloxy, 2,3-difluorophenoxy, 2,4-difluorophenoxy, 2,5-difluorophenoxy, 3,5-dimethoxyphenoxy, 3-dimethylaminophenoxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 3,4-dimethylbenzyl, 3,4-dimethylbenzyloxy, 3,5-dimethylbenzyloxy, 2,2-dimethylpropoxy, 1,3-dioxan-2-yl, 1,4-dioxan-2-yl, 1,3-dioxolan-2-yl, ethoxy, 4-ethoxyphenoxy, 4-ethylbenzyloxy, 3-ethylphenoxy, 4-ethylaminophenoxy, 3-ethyl-5-methylphenoxy, fluoro, 4-fluoro-3-methylbenzyl, 4-fluoro-3-methylphenyl, 4-fluoro-3-methylbenzoyl, 4-fluorobenzyloxy, 2-fluoro-3-methylphenoxy, 3-fluoro-4-methylphenoxy, 3-fluorophenoxy, 3-fluoro-2-nitrophenoxy, 2-fluoro-3-trifluoromethylbenzyloxy, 3-fluoro-5-trifluoromethylbenzyloxy, 4-fluoro-2-trifluoromethylbenzyloxy, 4-fluoro-3-trifluoromethylbenzyloxy, 2-fluorophenoxy, 4-fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2-fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4-trifluoromethylphenoxy,

4-fluoropyrid-2-yloxy, 2-furyl, 3-furyl, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, 2-hydroxy-3,3,3-trifluoropropoxy, 3-iodobenzyloxy, isobutyl, isobutylamino, isobutoxy, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, isopropoxy, isopropyl, 4-isopropylbenzyloxy, 3-isopropylphenoxy, 4-isopropylphenoxy, isopropylthio, 4-isopropyl-3-methylphenoxy, 3-isothiazolyl, 4-isothiazolyl, 5-isothiazolyl, 3-methoxybenzyl, 4-methoxycarbonylbutoxy, 3-methoxycarbonylprop-2-enyloxy, 4-methoxyphenyl, 3-methoxyphenylamino, 4-methoxyphenylamino, 3-methylbenzyloxy, 4-methylbenzyloxy, 3-methylphenoxy, 3-methyl-4-methylthiophenoxy, 4-methylphenoxy, 1-methylpropoxy, 2-methylpyrid-5-yloxy, 4-methylthiophenoxy, 2-naphthyloxy, 2-nitrophenoxy, 4-nitrophenoxy, 3-nitrophenyl, 4-nitrophenylthio, 2-oxazolyl, 4-oxazolyl, 5-oxazolyl, pentafluoroethyl, pentafluoroethylthio, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, phenoxy, phenylamino, 1-phenylethoxy, phenylsulfonyl, 4-propanoylphenoxy, propoxy, 4-propylphenoxy, 4-propoxyphenoxy, thiophen-3-yl, *sec*-butyl, 4-*sec*-butylphenoxy,*tert*-butoxy, 3-*tert*-butylphenoxy, 4-*tert*-butylphenoxy, 1,1,2,2-tetrafluoroethoxy, tetrahydrofuran-2-yl, 2-(5,6,7,8-tetrahydronaphthyloxy), thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, thiophen-2-yl, 2,3,5-trifluorobenzyloxy, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, 3,3,3-trifluoro-2-hydroxypropyl, trifluoromethoxy, 3-trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, 3-trifluoromethoxyphenoxy, 4-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 4-trifluoromethylbenzyloxy, 2,4-bis-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, 3-trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3-trifluoromethylphenyl, 3-trifluoromethylthiobenzyloxy, 4-trifluoromethylthiobenzyloxy, 2,3,4-trifluorophenoxy, 2,3,4-trifluorophenyl, 2,3,5-trifluorophenoxy, 3,4,5-trimethylphenoxy, 3-difluoromethoxyphenoxy, 3-pentafluoroethylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 3-trifluoromethylthiophenoxy, and trifluoromethylthio;

R_6, R_{11}, R_{31}, and R_{32} are independently selected from the group consisting of chloro, fluoro, hydrido, pentafluoroethyl, 1,1,2,2-tetrafluoroethoxy, trifluoromethyl, and trifluoromethoxy;

R_7 is selected from the group consisting of hydrido, fluoro, and trifluoromethyl;

R_{30} is selected from the group consisting of chloro, ethoxy, ethyl, fluoro, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, isobutyl, isobutoxy, isopropoxy, isopropyl, isopropylthio, methyl, pentafluoroethyl, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, propoxy, propyl, *sec*-butyl, *tert*-butoxy, 1,1,2,2-tetrafluoroethoxy, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, trifluoromethoxy, and trifluoromethyl.

15. The compound as recited in Claim 14 or a pharmaceutically acceptable salt thereof, wherein;

n is the integer 1;

A is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 4-methylcyclohexyl, 4-chloro-3-ethylphenoxycyclohexyl, 3-trifluoromethoxyphenoxycyclohexyl, 3-trifluoromethylcyclohexyl, 4-trifluoromethylcyclohexyl, 3,5-bis-trifluoromethylcyclohexyl, adamantyl, 3-trifluoromethyladamantyl, norbornyl, 3-trifluoromethylnorbornyl, norbornenyl, 7-oxabicyclo[2.2.1]heptan-2-yl, bicyclo[3.1.0]hexan-6-yl, cycloheptyl, cyclooctyl, 2-morpholinyl, 3-morpholinyl, 4-morpholinyl, 1-piperazinyl, 2-piperazinyl, 1-piperidinyl, 2-piperidinyl, 3-piperidinyl, 4-piperidinyl, 1-pyrrolidinyl, 2-pyrrolidinyl, 3-pyrrolidinyl, 2-dioxanyl, 4H-2-pyranyl, 4H-3-pyranyl, 4H-4-pyranyl, 4H-pyran-4-one-2-yl, 4H-pyran-4-one-3-yl, 2-tetrahydrofuranyl, 3-tetrahydrofuranyl, 2-tetrahydropyranyl, 3-tetrahydropyranyl, 4-tetrahydropyranyl, 2-tetrahydrothienyl, and 3-tetrahydrothienyl, wherein each ring carbon may be optionally substituted with R_{30}, a ring carbon other than the ring carbon at the point of attachment of A to Z may be optionally

substituted with oxo provided that no more than one ring carbon is substituted by oxo at the same time, ring carbon and nitrogen atoms adjacent to the carbon atom at the point of attachment may be optionally substituted with R_9 or R_{13}, a ring carbon or nitrogen atom adjacent to the R_9 position and two atoms from the point of attachment may be substituted with R_{10}, a ring carbon or nitrogen atom adjacent to the R_{13} position and two atoms from the point of attachment may be substituted with R_{12}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{10} position may be substituted with R_{11}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{12} position may be substituted with R_{32}, and a ring carbon or nitrogen atom four atoms from the point of attachment and adjacent to the R_{11} and R_{32} positions may be substituted with R_{31};

D_1, D_2, J_1, J_2 and K_1 are independently selected from the group consisting of C, N, O, S and a covalent bond to form the group consisting of 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrrolyl, 3-pyrrolyl, 2-imidazolyl, 4-imidazolyl, 3-pyrazolyl, 4-pyrazolyl, 2-oxazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl, 4-pyridazinyl, 1,3,5-triazin-2-yl, 1-indolizinyl, 7-indolizinyl, 1-isoquinolyl, and 2-quinolyl, wherein a ring carbon atom adjacent to the carbon atom at the point of attachment may be optionally substituted with R_4 or R_8, a ring carbon atom adjacent to the R_4 position and two atoms from the point of attachment may be substituted with R5, a ring carbon atom adjacent to the R_8 position and two atoms from the point of attachment may be substituted with R_7, and a ring carbon atom three atoms

from the point of attachment and adjacent to the R_5 and R_7 positions may be substituted with R_6;

R_1 is selected from the group consisting of trifluoromethyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, difluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

R_2 is selected from the group consisting of hydrido, methyl, ethyl, phenyl, 4-trifluoromethylphenyl, trifluoromethoxymethyl, 1,1,2,2-tetrafluoroethoxymethyl, difluoromethyl, pentafluoroethyl, trifluoromethyl, and 2,2,3,3,3-pentafluoropropyl;

R_3 is selected from the group consisting of hydrido, phenyl, 4-trifluoromethylphenyl, methyl, trifluoromethyl, difluoromethyl, and chlorodifluoromethyl;

Y and Z are independently selected from a covalent single bond and methylene;

R_4 and R_8 are independently selected from the group consisting of hydrido and fluoro;

R_9 and R_{13} are fluoro;

R_5, R_{10} and R_{12} are independently selected from the group consisting of benzyloxy, 5-bromo-2-fluorophenoxy, 4-bromo-3-fluorophenoxy, 3-bromobenzyloxy, 4-bromophenoxy,4-butoxyphenoxy, 3-chlorobenzyloxy, 2-chlorophenoxy, 4-chloro-3-ethylphenoxy, 4-chloro-3-methylphenoxy, 2-chloro-4-fluorophenoxy, 4-chloro-2-fluorophenoxy, 4-chlorophenoxy, 3-chloro-4-ethylphenoxy, 3-chloro-4-methylphenoxy, 3-chloro-4-fluorophenoxy, 4-chloro-3-fluorophenoxy, 4-chlorophenylamino, 5-chloropyrid-3-yloxy, cyclobutoxy, cyclobutyl, cyclohexylmethoxy, cyclopentoxy, cyclopentyl, cyclopentylcarbonyl, cyclopropylmethoxy, 2,3-dichlorophenoxy, 2,4-dichlorophenoxy, 2,4-dichlorophenyl, 3,5-dichlorophenyl, 3,5-dichlorobenzyl, 3,4-dichlorophenoxy, 3,4-difluorophenoxy,2,3-difluorobenzyloxy, 3,5-difluorobenzyloxy, difluoromethoxy, 3,5-difluorophenoxy, 3,4-difluorophenyl,

2,3-difluorophenoxy, 2,4-difluorophenoxy, 2,5-difluorophenoxy, 3,5-dimethoxyphenoxy,3-dimethylaminophenoxy, 3,4-dimethylbenzyloxy, 3,5-dimethylbenzyloxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 1,3-dioxolan-2-yl, 3-ethylbenzyloxy, 3-ethylphenoxy, 4-ethylaminophenoxy, 3-ethyl-5-methylphenoxy, 4-fluoro-3-methylbenzyl, 4-fluorobenzyloxy, 2-fluoro-3-methylphenoxy, 3-fluoro-4-methylphenoxy, 3-fluorophenoxy, 3-fluoro-2-nitrophenoxy, 2-fluoro-3-trifluoromethylbenzyloxy, 3-fluoro-5-trifluoromethylbenzyloxy, 2-fluorophenoxy, 4-fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2-fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4-trifluoromethylphenoxy, 2-furyl, 3-furyl, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, 2-hydroxy-3,3,3-trifluoropropoxy, isobutoxy, isobutyl, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, isopropoxy, 3-isopropylbenzyloxy, 3-isopropylphenoxy, isopropylthio, 4-isopropyl-3-methylphenoxy, 3-isothiazolyl, 4-isothiazolyl, 5-isothiazolyl, 3-methoxybenzyl, 4-methoxyphenylamino, 3-methylbenzyloxy, 4-methylbenxyloxy, 3-methylphenoxy, 3-methyl-4-methylthiophenoxy, 4-methylphenoxy, 1-methylpropoxy, 2-methylpyrid-5-yloxy, 4-methylthiophenoxy, 2-naphthyloxy, 2-nitrophenoxy, 4-nitrophenoxy, 3-nitrophenyl, 2-oxazolyl, 4-oxazolyl, 5-oxazolyl, pentafluoroethyl, pentafluoroethylthio, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, phenoxy, phenylamino, 1-phenylethoxy, 4-propylphenoxy, 4-propoxyphenoxy, thiophen-3-yl,tert -butoxy, 3-tert -butylphenoxy, 4-tert -butylphenoxy, 1,1,2,2-tetrafluoroethoxy, tetrahydrofuran-2-yl, 2-(5,6,7,8-tetrahydronaphthyloxy), thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, thiophen-2-yl, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, 3,3,3-trifluoro-2-hydroxypropyl, trifluoromethoxy, 3-trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, 4-trifluoromethoxyphenoxy, 3-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, 3-trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3-trifluoromethylphenyl, 2,3,4-trifluorophenoxy, 2,3,5-trifluorophenoxy, 3,4,5-trimethylphenoxy, 3-difluoromethoxyphenoxy, 3-pentafluoroethylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy,

3-trifluoromethylthiophenoxy, 3-trifluoromethylthiobenzyloxy, and trifluoromethylthio;

R_6, R_{11}, R_{31}, and R_{32} are independently selected from the group consisting of chloro, fluoro, hydrido, pentafluoroethyl, 1,1,2,2-tetrafluoroethoxy, and trifluoromethyl;

R_7 is selected from the group consisting of hydrido, fluoro, and trifluoromethyl;

R_{30} is selected from the group consisting of chloro, ethyl, fluoro, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, isobutyl, isopropyl, methyl, pentafluoroethyl, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, propyl, *sec*-butyl, 1,1,2,2-tetrafluoroethoxy, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, trifluoromethoxy, and trifluoromethyl.

16. The compound as recited in Claim 15 or a pharmaceutically acceptable salt thereof, wherein;

n is the integer 1;

A is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 4-methylcyclohexyl, 4-chloro-3-ethylphenoxycyclohexyl, 3-trifluoromethoxyphenoxycyclohexyl, 3-trifluoromethylcyclohexyl, 4-trifluoromethylcyclohexyl, 3,5-bis-trifluoromethylcyclohexyl, adamantyl, 3-trifluoromethyladamantyl, norbornyl, 3-trifluoromethylnorbornyl, norbornenyl, 7-oxabicyclo[2.2.1]heptan-2-yl, bicyclo[3.1.0]hexan-6-yl, 2-tetrahydrofuranyl, 3-tetrahydrofuranyl, 2-tetrahydropyranyl, 3-tetrahydropyranyl, 4-tetrahydropyranyl, 2-tetrahydrothienyl, and 3-tetrahydrothienyl, wherein a ring carbon other than the ring carbon at the point of attachment of A to Z may be optionally substituted with oxo provided that no more than one ring carbon is substituted by oxo at the same time, ring carbon and nitrogen atoms adjacent to the carbon atom at the point of attachment may be optionally substituted with R_9 or R_{13}, a ring carbon or nitrogen atom adjacent to the R_9 position and two atoms from the

point of attachment may be substituted with R_{10}, a ring carbon or nitrogen atom adjacent to the R_{13} position and two atoms from the point of attachment may be substituted with R_{12}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{10} position may be substituted with R_{11}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{12} position may be substituted with R_{32}, and a ring carbon or nitrogen atom four atoms from the point of attachment and adjacent to the R_{11} and R_{32} positions may be substituted with R_{31};

D_1, D_2, J_1, J_2 and K_1 are independently selected from the group consisting of C, N, O, S and a covalent bond to form the group consisting of 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrrolyl, 3-pyrrolyl, 2-imidazolyl, 4-imidazolyl, 3-pyrazolyl, 4-pyrazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl, 4-pyridazinyl, and 1,3,5-triazin-2-yl, wherein a ring carbon atom adjacent to the carbon atom at the point of attachment may be optionally substituted with R_4 or R_8, a ring carbon atom adjacent to the R_4 position and two atoms from the point of attachment may be substituted with R5, a ring carbon atom adjacent to the R_8 position and two atoms from the point of attachment may be substituted with R_7, and a ring carbon atom three atoms from the point of attachment and adjacent to the R_5 and R_7 positions may be substituted with R_6;

R_1 is selected from the group consisting of trifluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

R_2 is hydrido, pentafluoroethyl, and trifluoromethyl;

R_3 is selected from the group consisting of hydrido, methyl, trifluoromethyl, and difluoromethyl

Y is a covalent single bond;

Z is methylene;

R_4 and R_8 are independently selected from the group consisting of hydrido and fluoro;

R_9 and R_{13} are fluoro;

R_5, R_{10} and R_{12} are independently selected from the group consisting of 5-bromo-2-fluorophenoxy, 4-chloro-3-ethylphenoxy, cyclopentyl, 2,3-dichlorophenoxy, 3,4-dichlorophenoxy, 3-difluoromethoxyphenoxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 3-ethylphenoxy, 3-ethyl-5-methylphenoxy, 4-fluoro-3-methylphenoxy, 4-fluorophenoxy, 2-furyl, isobutyl, isopropoxy, 3-isopropylphenoxy, 3-methylphenoxy, pentafluoroethyl, 3-pentafluoroethylphenoxy, 3-tert -butylphenoxy, 1,1,2,2-tetrafluoroethoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 2-(5,6,7,8-tetrahydronaphthyloxy),trifluoromethoxy, 3-trifluoromethoxybenzyloxy,3-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, trifluoromethylthio, and 3-trifluoromethylthiophenoxy;

R_6, R_{11}, R_{31}, and R_{32} are independently selected from the group consisting of chloro, fluoro, hydrido, pentafluoroethyl, 1,1,2,2-tetrafluoroethoxy, and trifluoromethyl;

R_7 is selected from the group consisting of hydrido and fluoro.

17. The compound as recited in Claim 15 or a pharmaceutically acceptable salt thereof, wherein;

n is the integer 1;

A is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 4-methylcyclohexyl, 4-chloro-3-ethylphenoxycyclohexyl, 3-trifluoromethoxyphenoxycyclohexyl, 3-

trifluoromethylcyclohexyl, 4-trifluoromethylcyclohexyl, 3,5-bis-trifluoromethylcyclohexyl, adamantyl, 3-trifluoromethyladamantyl, norbornyl, 3-trifluoromethylnorbornyl, norbornenyl, 7-oxabicyclo[2.2.1]heptan-2-yl, bicyclo[3.1.0]hexan-6-yl, 2-tetrahydrofuranyl, 3-tetrahydrofuranyl, 2-tetrahydropyranyl, 3-tetrahydropyranyl, 4-tetrahydropyranyl, 2-tetrahydrothienyl, and 3-tetrahydrothienyl, wherein a ring carbon other than the ring carbon at the point of attachment of A to Z may be optionally substituted with oxo provided that no more than one ring carbon is substituted by oxo at the same time, ring carbon and nitrogen atoms adjacent to the carbon atom at the point of attachment may be optionally substituted with R_9 or R_{13}, a ring carbon or nitrogen atom adjacent to the R_9 position and two atoms from the point of attachment may be substituted with R_{10}, a ring carbon or nitrogen atom adjacent to the R_{13} position and two atoms from the point of attachment may be substituted with R_{12}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{10} position may be substituted with R_{11}, a ring carbon or nitrogen atom three atoms from the point of attachment and adjacent to the R_{12} position may be substituted with R_{32}, and a ring carbon or nitrogen atom four atoms from the point of attachment and adjacent to the R_{11} and R_{32} positions may be substituted with R_{31};

D_1, D_2, J_1, J_2 and K_1 are independently selected from the group consisting of C, N, O, S and a covalent bond to form the group consisting of 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 2-pyrrolyl, 3-pyrrolyl, 2-imidazolyl, 4-imidazolyl, 3-pyrazolyl, 4-pyrazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl, 4-pyridazinyl, and 1,3,5-triazin-2-yl, wherein a ring carbon atom adjacent to the carbon atom at the point of attachment may be optionally substituted with R_4 or R_8, a ring carbon atom adjacent to the R_4 position and two atoms from the point of attachment may be substituted with

R5, a ring carbon atom adjacent to the R_8 position and two atoms from the point of attachment may be substituted with R_7, and a ring carbon atom three atoms from the point of attachment and adjacent to the R_5 and R_7 positions may be substituted with R_6;

R_1 is selected from the group consisting of trifluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

R_2 is hydrido, pentafluoroethyl, and trifluoromethyl;

R_3 is selected from the group consisting of hydrido, methyl, trifluoromethyl, and difluoromethyl

Y is methylene;

Z is a covalent single bond;

R_4 and R_8 are independently selected from the group consisting of hydrido and fluoro;

R_9 and R_{13} are fluoro;

R_5, R_{10} and R_{12} are independently selected from the group consisting of 5-bromo-2-fluorophenoxy, 4-chloro-3-ethylphenoxy, cyclopentyl, 2,3-dichlorophenoxy, 3,4-dichlorophenoxy, 3-difluoromethoxyphenoxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 3-ethylphenoxy, 3-ethyl-5-methylphenoxy, 4-fluoro-3-methylphenoxy, 4-fluorophenoxy, 2-furyl, isobutyl, isopropoxy, 3-isopropylphenoxy, 3-methylphenoxy, pentafluoroethyl, 3-pentafluoroethylphenoxy, 3-tert -butylphenoxy, 1,1,2,2-tetrafluoroethoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 2-(5,6,7,8-tetrahydronaphthyloxy),trifluoromethoxy, 3-trifluoromethoxybenzyloxy,3-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, trifluoromethylthio, and 3-trifluoromethylthiophenoxy;

R_6, R_{11}, R_{31}, and R_{32} are independently selected from the group consisting of chloro, fluoro, hydrido, pentafluoroethyl, 1,1,2,2-tetrafluoroethoxy, and trifluoromethyl;

R_7 is selected from the group consisting of hydrido and fluoro.

18. A compound as recited in Claim 1, or a pharmaceutically acceptable salt thereof, wherein said compound is selected from the group consisting of:

3-[[3-(4-chloro-3-ethylphenoxy)phenyl](cyclohexylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(4-chloro-3-ethylphenoxy)phenyl](cyclopentylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(4-chloro-3-ethylphenoxy)phenyl](cyclopropylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(4-chloro-3-ethylphenoxy)phenyl][(3-trifluoromethyl)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(4-chloro-3-ethylphenoxy)phenyl][(3-pentafluoroethyl)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(4-chloro-3-ethylphenoxy)phenyl][(3-trifluoromethoxy)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(4-chloro-3-ethylphenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)cyclo-hexylmethyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethoxyphenoxy)phenyl](cyclohexylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethoxyphenoxy)phenyl](cyclopentylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[33-trifluoromethoxyphenoxy)phenyl](cyclopropylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethoxyphenoxy)phenyl][(3-trifluoromethyl)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethoxyphenoxy)phenyl][(3-pentafluoroethyl)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethoxyphenoxy)phenyl][(3-trifluoromethoxy)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethoxyphenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)cyclo-hexylmethyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-isopropylphenoxy)phenyl](cyclohexylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-isopropylphenoxy)phenyl](cyclopentylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-isopropylphenoxy)phenyl](cyclopropylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-isopropylphenoxy)phenyl][(3-trifluoromethyl)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-isopropylphenoxy)phenyl][(3-pentafluoroethyl)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-isopropylphenoxy)phenyl][(3-trifluoromethoxy)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-isopropylphenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)cyclo-hexyl]methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(2,3-dichlorophenoxy)phenyl](cyclohexylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(2,3-dichlorophenoxy)phenyl](cyclopentylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(2,3-dichlorophenoxy)phenyl](cyclopropylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(2,3-dichlorophenoxy)phenyl][(3-trifluoromethyl)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(2,3-dichlorophenoxy)phenyl][(3-pentafluoroethyl)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(2,3-dichlorophenoxy)phenyl][(3-trifluoromethoxy)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(2,3-dichlorophenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)cyclo-hexylmethyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(4-fluorophenoxy)phenyl](cyclohexylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(4-fluorophenoxy)phenyl](cyclopentylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(4-fluorophenoxy)phenyl](cyclopropylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(4-fluorophenoxy)phenyl](3-trifluoromethyl)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(4-fluorophenoxy)phenyl](3-pentafluoroethyl)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(4-fluorophenoxy)phenyl][(3-trifluoromethoxy)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(4-fluorophenoxy)phenyl][3-(1,1,2,2-tetrafluoroethoxy)cyclo-hexylmethyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethoxybenzyloxy)phenyl](cyclohexylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethoxybenzyloxy)phenyl](cyclopentylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethoxybenzyloxy)phenyl](cyclopropylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethoxybenzyloxy)phenyl][(3-trifluoromethyl)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethoxybenzyloxy)phenyl][(3-pentafluoroethyl)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethoxybenzyloxy)phenyl][(3-trifluoromethoxy)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethoxybenzyloxy)phenyl][3-(1,1,2,2-tetrafluoroethoxy)-cyclohexylmethyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethylbenzyloxy)phenyl](cyclohexylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethylbenzyloxy)phenyl](cyclopentylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethylbenzyloxy)phenyl](cyclopropylmethyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethylbenzyloxy)phenyl][(3-trifluoromethyl)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethylbenzyloxy)phenyl][(3-pentafluoroethyl)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethylbenzyloxy)phenyl][(3-trifluoromethoxy)cyclohexyl-methyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[3-(3-trifluoromethylbenzyloxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)cyclo-hexylmethyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethyl)phenyl]methyl](cyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-pentafluoroethyl)phenyl]methyl](cyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethoxy)phenyl]methyl](cyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl](cyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethyl)phenyl]methyl](4-methylcyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-pentafluoroethyl)phenyl]methyl](4-methylcyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethoxy)phenyl]methyl](4-methylcyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl](4-methylcyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethyl)phenyl]methyl](3-trifluoromethylcyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-pentafluoroethyl)phenyl]methyl](3-trifluoromethylcyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethoxy)phenyl]methyl](3-trifluoromethylcyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl](3-trifluoromethylcyclo-hexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethyl)phenyl]methyl][3-(4-chloro-3-ethylphenoxy)cyclo-hexyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-pentafluoroethyl)phenyl]methyl][3-(4-chloro-3-ethylphenoxy)cyclohexyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethoxy)phenyl]methyl][3-(4-chloro-3-ethylphenoxy)cyclo-hexyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl] [3-(4-chloro-3-ethylphenoxy)-cyclohexyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethyl)phenyl]methyl](3-phenoxycyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-pentafluoroethyl)phenyl]methyl](3-phenoxycyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethoxy)phenyl]methyl](3-phenoxycyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl](3-phenoxycyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethyl)phenyl]methyl](3-isopropoxycyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-pentafluoroethyl)phenyl]methyl](3-isopropoxycyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethoxy)phenyl]methyl](3-isopropoxycyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl](3-isopropoxycyclohexyl)-amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethyl)phenyl]methyl](3-cyclopentyloxycyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-pentafluoroethyl)phenyl]methyl](3-cyclopentyloxycyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethoxy)phenyl]methyl](3-cyclopentyloxycyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl](3-cyclopentyloxycyclohexyl)-amino]-1,1,1-trifluoro-2-propanol;

3-[[[(2-trifluoromethyl)pyrid-6-yl]methyl](3-isopropoxycyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(2-trifluoromethyl)pyrid-6-yl]methyl](3-cyclopentyloxycyclohexyl)-amino]-1,1,1-trifluoro-2-propanol;

3-[[[(2-trifluoromethyl)pyrid-6-yl]methyl](3-phenoxycyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(2-trifluoromethyl)pyrid-6-yl]methyl](3-trifluoromethylcyclohexyl)amino]-1,1,1-trifluoro-2-propanol;

3-[[[(2-trifluoromethyl)pyrid-6-yl]methyl][3-(4-chloro-3-ethylphenoxy)cyclo-hexyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[[(2-trifluoromethyl)pyrid-6-yl]methyl][3-(1,1,2,2-tetrafluoroethoxy)cyclo-hexyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[[(2-trifluoromethyl)pyrid-6-yl]methyl](3-pentafluoroethylcyclohexyl)-amino]-1,1,1-trifluoro-2-propanol;

3-[[[(2-trifluoromethyl)pyrid-6-yl]methyl](3-trifluoromethoxycyclohexyl)-amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethyl)phenyl]methyl][3-(4-chloro-3-ethylphenoxy)propyl]-amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-pentafluoroethyl)phenyl]methyl][3-(4-chloro-3-ethylphenoxy)propyl]-amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethoxy)phenyl]methyl][3-(4-chloro-3-ethylphenoxy)propyl]-amino]-1,1,1-trifluoro-2-propanol;

3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl] [3-(4-chloro-3-ethylphenoxy)-propyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethyl)phenyl]methyl][3-(4-chloro-3-ethylphenoxy)-2,2,-di-fluroropropyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-pentafluoroethyl)phenyl]methyl][3-(4-chloro-3-ethylphenoxy)-2,2,-di-fluroropropyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethoxy)phenyl]methyl][3-(4-chloro-3-ethylphenoxy)-2,2,-di-fluroropropyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl] [3-(4-chloro-3-ethylphenoxy)- 2,2,-difluroropropyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethyl)phenyl]methyl][3-(isopropoxy)propyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-pentafluoroethyl)phenyl]methyl][3-(isopropoxy)propyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[[(3-trifluoromethoxy)phenyl]methyl][3-(isopropoxy)propyl]amino]-1,1,1-trifluoro-2-propanol;

3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl][3-(isopropoxy)propyl]amino] -1,1,1-trifluoro-2-propanol; and

3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl][3-(phenoxy)propyl]amino] -1,1,1-trifluoro-2-propanol.

19. A pharmaceutical composition comprising a compound of one of claims 1 through 18 together with a pharmaceutically acceptable carrier.

20. A method of treating coronary artery disease or other CETP-mediated disorders in a subject by administering a therapeutically effective amount of a compound of one of claims 1 through 18.

21. A method of preventing coronary artery disease or other CETP-mediated disorders in a subject by administering a therapeutically effective amount of a compound of one of claims 1 through 18.

22. A method of treating or preventing cerebral vascular accident (CVA) or other CETP-mediated disorders in a subject by administering a therapeutically effective amount of a compound of one of claims 1 through 18.

23. A method of treating or preventing dyslipidemia and other CETP-mediated disorders in a subject by administering a therapeutically effective amount of a compound of one of claims 1 through 18.

INTERNATIONAL SEARCH REPORT

Interr nal Application No
PCT/US 99/22123

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07C217/52 C07C215/16 C07C215/76 C07C215/50 C07C217/82
C07C217/54 C07D213/74 C07D309/14 A61K31/135 A61K31/33

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07C C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2 700 686 A (JOSEPH B. DICKEY ET AL.) 25 January 1955 (1955-01-25) cited in the application column 12-13; examples 22-29 ---	1
A	DUNN C ET AL: "THE SYNTHESIS OF FLUORINE-CONTAINING PTERINS" TETRAHEDRON,NL,ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, vol. 52, no. 40, page 13017-13026 XP002063653 ISSN: 0040-4020 page 13024, paragraph 2 ---	1
A	WO 96 04249 A (STANFORD RES INST INT ;UNIV GLASGOW (GB); CANCER RES CAMPAIGN TECH) 15 February 1996 (1996-02-15) claims 12,13,16 ---	1
	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
12 January 2000	21/01/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Rufet, J

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Intern al Application No
PCT/US 99/22123

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 801 060 A (PFIZER) 15 October 1997 (1997-10-15) cited in the application abstract	1,19-23
A	GB 2 305 665 A (MERCK & CO INC) 16 April 1997 (1997-04-16) cited in the application abstract; claims 1-17	1,19-23
A	EP 0 818 197 A (BAYER AG) 14 January 1998 (1998-01-14) cited in the application abstract; claim 1	1,19-23

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/22123

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 20-23
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 20-23 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.: 1-19
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-19

Present claims 1-19 relate to an extremely large number of possible compounds/compositions.
In fact, the claims contain so many options, variables and provisos that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and/or concise), namely the formula (I) of claim 1 wherein:

R1 = CF3
R2 = R3 = Hydrogen
Z = Y = CH2 or bond
A = aromatic ring AQ1 with free sites (R4-R8)
the other ring Q attached via Y on the Nitrogen atom is a cycloalkyl ring, a condensed polycycloalkyl ring, or an alkyl, alkenyl or alkynyl group with free sites.

It is stressed that this scope covers the majority of the examples.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

.ormation on patent family members

Intern ıal Application No
PCT/US 99/22123

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2700686 A	25-01-1955	NONE	
WO 9604249 A	15-02-1996	US 5721265 A	24-02-1998
		CA 2196900 A	15-02-1996
		EP 0775117 A	28-05-1997
		JP 10506104 T	16-06-1998
EP 0801060 A	15-10-1997	CA 2201988 A	09-10-1997
		JP 10036348 A	10-02-1998
		US 5843972 A	01-12-1998
GB 2305665 A	16-04-1997	US 5714506 A	03-02-1998
EP 0818197 A	14-01-1998	DE 19627431 A	15-01-1998
		BG 101748 A	30-04-1998
		BR 9703890 A	03-11-1998
		CA 2209825 A	08-01-1998
		CN 1174196 A	25-02-1998
		CZ 9702144 A	14-01-1998
		HR 970333 A	30-04-1998
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		PL 320953 A	19-01-1998
		SG 46781 A	20-02-1998
		SK 92597 A	06-05-1998
		US 5932587 A	03-08-1999